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CLINICAL PATTERNS AND SEASONAL TRENDS IN RESPIRATORY SYNCYTIAL VIRUS HOSPITALIZATIONS IN SÃO PAULO, BRAZIL*

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SUMMARY

The respiratory viruses are recognized as the most frequent lower respiratory tract pathogens for infants and young children in developed countries but less is known for developing populations. The authors conducted a prospective study to evaluate the occurrence, clinical patterns, and seasonal trends of viral infections among hospitalized children with lower respiratory tract disease (Group A). The presence of respiratory viruses in children's nasopharyngeal was assessed at admission in a pediatric ward. Cell cultures and immunofluorescence assays were used for viral identification. Complementary tests included blood and pleural cultures conducted for bacterial investigation. Clinical data and radiological exams were recorded at admission and throughout the hospitalization period. To better evaluate the results, a non- respiratory group of patients (Group B) was also constituted for comparison. Starting in February 1995, during a period of 18 months, 414 children were included- 239 in Group A and 175 in Group B. In Group A, 111 children (46.4%) had 114 viruses detected while only 5 children (2.9%) presented viruses in Group B. Respiratory Syncytial Virus was detected in 100 children from Group A (41.8%), Adenovirus in 11 (4.6%), Influenza A virus in 2 (0.8%), and Parainfluenza virus in one child (0.4%). In Group A, aerobic bacteria were found in 14 cases (5.8%). Respiratory Syncytial Virus was associated to other viruses and/or bacteria in six cases. There were two seasonal trends for Respiratory Syncytial Virus cases, which peaked in May and June. All children affected by the virus were younger than 3 years of age, mostly less than one year old. Episodic diffuse bronchial commitment and/or focal alveolar condensation were the clinical patterns more often associated to Respiratory Syncytial Virus cases. All children from Group A survived. In conclusion, it was observed that Respiratory Syncytial Virus was the most frequent pathogen found in hospitalized children admitted for severe respiratory diseases. Affected children were predominantly infants and boys presenting bronchiolitis and focal pneumonias. Similarly to what occurs in other subtropical regions, the virus outbreaks peak in the fall and their occurrence extends to the winter, which parallels an increase in hospital admissions due to respiratory diseases.

KEYWORDS: Brazil; Children; Morbidity; Pneumonia, Epidemiology; Pneumonia, mortality; Respiratory syncytial virus.

INTRODUCTION

The respiratory syncytial virus (RSV) is recognized as the single most frequent lower respiratory tract pathogen in infants and young children in developed countries but less is known for populations of developing countries[5,14,37]. RSV activity in the United States is monitored by the National Respiratory and Enteric Virus Surveillance System, a voluntary laboratory-based system started in 1990, but there is not a similar epidemiological system operating in developing countries, as yet[4].

Severe RSV infections may occur in previously healthy infants and young children, although prematures and patients affected by cardiac, pulmonary, or immune system disturbances are at greatest risk[18,19,26]. RSV infections are, therefore, a common cause of pediatric hospitalization in developed countries[20,21,27]. Since low socioeconomic conditions constitute a recognized risk factor for RSV bronchiolitis and pneumonia in developed countries, the role of the virus as a respiratory pathogen should be better evaluated in developing countries as well[17,20,24].

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RSV infections present seasonal incidence. There are outbreaks associated with increased rates of hospitalization and death from lower respiratory tract illness (LRI)[1,20,32]. In temperate climates, RSV usually causes yearly outbreaks in winter or early spring in the northern[16,38] and southern hemispheres, as observed in Santiago-Chile[2], Buenos Aires-Argentina[43], and Montevideo-Uruguay[35]. In regions with tropical and subtropical climates, like southeastern Brazil, RSV has occurred in the form of annual epidemics, peaking in the fall, in the months of May or June, as has been observed in Rio de Janeiro[33]. A better understanding of seasonal and clinical patterns of these yearly RSV outbreaks can lead to the improvement of medical diagnosis and treatment, especially for the more severe cases[6,41]. Prophylactic measures can also be better defined as a result of increased knowledge about the action of the virus[29].

In the present study, we determined the frequencies, by age group, of RSV and other respiratory viruses detected in infants and young children admitted to a pediatric ward in São Paulo, Brazil. Seasonal and clinical patterns of severe RSV infections were evaluated in two consecutive seasons.

MATERIAL AND METHODS

Ethical guidelines: The present study was approved by the Ethical Comission of the University Hospital. Inform consent was obtained from parents or legal guardians of participants.

Patient selection: Children younger than 15 years of age admitted to the ward of the Pediatric Clinic of the University Hospital, University of São Paulo, were eligible for inclusion in the study regardless of diagnosis at admission. The Clinic provides care to low income children who live in the Butantã Health District, with a population of 400,000 inhabitants. From March 1995 to March 1996, the first two patients admitted each day, Monday to Thursday, were enrolled. In addition to that, from April to August 1996, the study included all patients admitted in that same period of the week.

Nasopharyngeal aspirates (NPA) and swabs (NPS) were obtained from each child at the time of hospital admission for respiratory virus diagnosis[41,42]. The diagnosis and clinical features were recorded at the time of admission and the clinical course was monitored during the hospital[6,15,40].

Virological studies: Clinical specimens - NPAs were collected by vacuum suction through a plastic catheter with a specimen trap. Approximately 3 ml of transport medium (phosphate-buffered saline solution, with 0.5% gelatin) was suctioned through the catheter into the trap and transported within 1 to 2 hours on wet ice to the laboratory. NPSs were placed in tubes with 2 ml of the same transport medium. All clinical specimens were analyzed for verification of the presence of respiratory viruses at the Laboratories of Clinical and Molecular Virology of the Department of Microbiology, Institute of Biomedical Sciences, University of São Paulo[42].

Viral isolation - All specimens were processed on the same day they were collected. NPAs were mechanically agitated, treated with antibiotics for 30 minutes, and centrifuged at 1,500 rpm. Supernatants of 0.1 ml were inoculated into 2 monolayer wells each of Hep-2, NCI-H292 and HeLa I cells cultured in 24-well polystyrene microplates (Corning Inc^{R}., New York, NY). All cultures were incubated at 37 ^{o}C and examined every other day for cytopathic effect (CPE) for a period of 10 days. One or two cell medium passages were proceeded. The presence of respiratory viruses was confirmed by indirect immunofluorescence assay (IFA) for cultures with possible CPE, as well as for monolayers without CPE at the end of the observation period[42].

Indirect immunofluorescence assay (IFA) - For antigen detection of influenza viruses A and B, parainfluenza viruses 1, 2 and 3, RSV and Adenoviruses, smears were prepared on Teflon-covered glass slides containing 7mm diameter wells (Dynatech Laboratory Inc^{R}., Chantilly, Virginia) and fixed with cold acetone. IFA tests using monoclonal antibodies from the Respiratory Viruses Panel I Viral Screening & Identification Kit, kindly provided by David Beckman (Chemicon International Inc^{R}., Temecula, California), were performed on the same day according to manufacturer's instructions (Chemicon Light Diagnostics, Catalog no. 3105). Specimens were considered positive when smears showed green particulate cytoplasmic or nuclear fluorescence easily recognizable in three or more cells[42].

During the study period, and at the time of admission to the ward, venous blood samples were collected from all children included in the protocol for culture of aerobic bacteria in tryptic soy broth (TSB)[12,13]. The pleural liquid, when present, was also sent for identification of bacteria, by culture in TSB, as well as for direct bacterioscopic exam (Gram staining).

Statistical analysis - The comparison of proportions was performed with the Chi square test for categorical variables and Wilcoxon rank sum test for continuous variables. The Mann-Whitney test was used for the comparison of the averages. Analyses were performed with the Epi Info Software program, Version 6.03[7,25].

RESULTS

Clinical and laboratory findings for hospitalized children: During the 18-month study period, there were 1,810 admissions to the Pediatric Clinic, both to the ward and the intensive care unit, of which 836 (45.1%) presented lower respiratory diseases (LRD) as the cause for admission. The distribution of the cases during the period was not regular ($p < 0.0001$). The LRD hospitalized children presented an average of 46.4 cases/month in the period, with a higher average of admissions for LRD, 66.8 cases/month ($p = 0.02$), from May to September 1995, and from April to July 1996 (Table 1). There were 20 deaths during the period, averaging 1.1/month, corresponding to 2.3% of the LRD cases admitted in the period (Table 1).

According to the selection criteria of the study, 414 children were enrolled for virological investigation. In the initial period, from March 1995 to March 1996, 213 children were included and another 201 in the subsequent period, from April to August 1996. There were 251 (60.6%) boys and 163 (39.4%) girls including 27 (6.5%) neonates, 140 (33.8%) children aged from 1 to 5 months, 72 (17.4%) from 6 to 11 months, 126 (30.4%) from 1 to 4 years, and 49 (11.8%) from 5 to 14 years.

A total of 239 children (57.7%) presented LRD (Group A), and another 175 (42.3%) were admitted to the clinic without LRD (Group B). Among the children from Group A, there were 146 boys and 63 girls

Table 1
Monthly lower respiratory disease admissions and mortality in the period of study

Month	Patients	Deaths
Mar 95	21	1
Apr 95	37	0
May 95	80	0
Jun 95	85	2
Jul 95	64	2
Aug 95	73	3
Sept 95	49	1
Oct 95	34	0
Nov 95	20	1
Dec 95	30	0
Jan 96	21	2
Feb 96	17	2
Mar 96	33	1
Apr 96	66	1
May 96	77	2
Jun 96	58	1
Jul 96	50	0
Aug 96	21	1
Total	836	20

with LRD cases. Their median age was 10.5 months. The clinical diagnoses at admission were pneumonia (122 cases), pneumonia and wheezing (43), bronchiolitis (45), recurrent wheezing (27), atelectasis (1), and bronchiectasis (1). None of the children from Group A died during the study period. Viral agents were identified at admission in 111 (46.4%) children from Group A: one virus in 108 cases (45.2%) and two viruses in 3 (1.3%). RSV was identified in 100 children (41.8%), Adenovirus in 11 (4.6%), Influenza A in 2 (0.8%), and Parainfluenza 3 viruses in 1 child (0.4%) (Table 2).

The RSV significantly predominated over all the other viral agents in children up to four years of age, who are within the age group that concentrates almost all of the LRD cases. The highest RSV identification rates occurred in newborns with LRD (92.9%), and the agent was present in 86 (54.1%) of the under one-year-old with LRD (Table 2). From that age on up, the children presented a significantly lower percentage of RSV ($p < 0.0001$), and it was not identified in any child over 3 years of age. The predominance of RSV over the other viruses was less marked among the 1 to 4 year-olds, the age interval in which the virus was least found and the Adenovirus reached its highest frequency (Table 2). Also, the virus predominates mostly among boys (146:93). Under clinical diagnoses, RSV-infected patients were significantly more likely to present bronchiolitis or pneumonia with wheezing than with isolated pneumonia or recurrent wheezing (Table 3).

Table 3
Clinical diagnosis[E] of children at admission to a pediatric ward upon the presence of RSV at the upper airway

	RSV + N (%)*	RSV – N (%)*	TOTAL N (%)*
Pneumonia (@)	38 (31.1)	84 (68.9)	122 (100.0)
Bronchiolitis (#)	30 (66.7)	15 (33.3)	45 (100.0)
Pneumonia with wheezing (+)	22 (51.2)	21 (48.8)	43 (100.0)
Recurrent wheezing (&)	10 (37.0)	17 (63.0)	27 (100.0)
TOTAL	100 (42.2)	137 (58.8)	237 (100.0)

+ detected; - not detected; * of the line; E – excluded one case of atelectasis and one of bronchiectasis; (#) vs. (@), $p < 0.001$; (+) vs. (@), $p = 0.03$; (#) vs. (&), $p = 0.01$

The RSV case distribution in relation to the month of admission indicates that there were two epidemics during the study period, each lasting for about four months (Fig. 1). The first RSV outbreak occurred from May through August 1995, and the second from April through July 1996. During the months of May and June, when RSV was most prevalent, the proportion of RSV-LRD admissions ranged from 51% to 85%. The epidemics were simultaneous to the increase in LRD cases, as can be observed in Table 1.

The children from Group B, i.e., without LRD, presented median age of 26 months, and the male/female ratio was 1.5/1 (105:70). The clinical diagnoses at admission were of gastrointestinal disturbances in

Table 2
Virus identifications in children hospitalized with lower respiratory disease, by age group, São Paulo, Brazil, March 1995 through August 1996

	Number (%) of identifications by Age Group					
Results	< 1 month	1 – 5 months	6 – 11 months	1 – 4 years	5 – 14 years	Total
Children evaluate	14 (100.0)	93 (100.0)	52 (100.0)	62 (100.0)	8 (100.0)	239 (100.0)
Any virus identified	13 (92.9)	52 (55.9)	26 (50.0)	*19 (30.6)	1 (5.6)	111 (46.4)
Virus						
Respiratory syncytial virus	13 (92.9)	51 (54.8)	22 (42.3)	14 (22.6)	0 (0.0)	100 (41.8)
Adenovirus	0 (0.0)	1 (1.1)	4 (7.7)	6 (9.7)	0 (0.0)	11 (4.6)
Influenza A	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.6)	1 (5.6)	2 (0.8)
Parainfluenza virus 3	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.6)	0 (0.0)	1 (0.4)
Total	**13**	**52**	**26**	**22**	**1**	**114**

*Includes 2 patients with both RSV and adenovirus, and 1 patient with both RSV and influenza A.

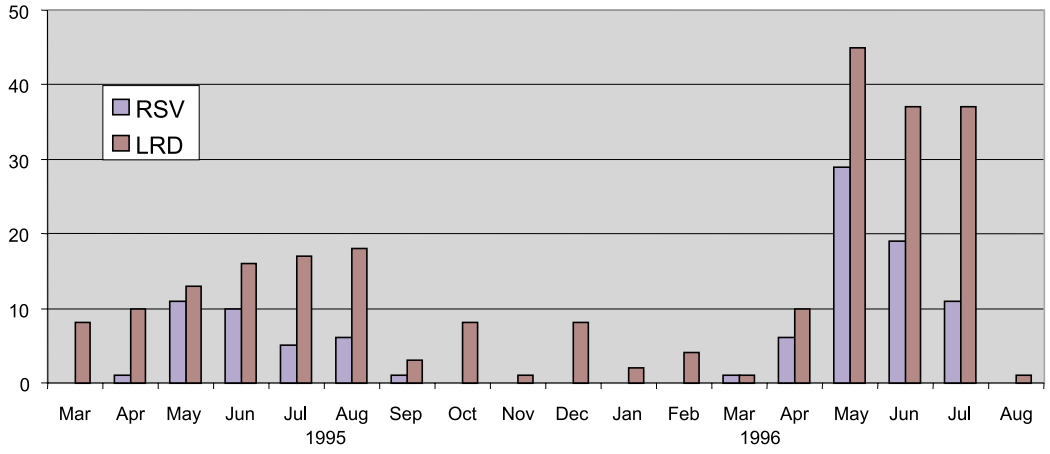

Fig. 1 - Seasonal trends in RSV identifications in children hospitalized with respiratory tract illness, São Paulo, Brazil, March 1995 through August 1996

72 cases (41.1%), central nervous system disturbances in 28 patients (16.0%), urinary diseases in 21 (12.0%), osteo-articular problems in 14 (8.0%), hematological diseases in 13 (7.4%), endocrine disorders in 12 (6.9%), skin diseases in 9 (5.2%), and cardiac problems in 6 (3.4%). Viruses were seldom identified at the upper airway in children without LRD. Among 175 children, Adenovirus was present in 5 (2.9%), RSV in 3 (1.7%), and Influenza A in just 1 (0.6%). Other respiratory viruses were not found. One patient from this group died during hospitalization.

The bacterial infections were studied in Group A, by the analyses of the blood cultures collected in all cases, of pleural liquid, in 15 cases, of serum samples for *Chlamydia trachomatis*, in 6 cases, by the study of the alcohol-acid resistant bacillus in the gastric secretion, in 9 cases, and by the culture of tracheal aspirate in the Loewenstein medium, in 5 of the cases. Bacterial infections were present in 14 children (5.8%), being the single pathogens identified in 10 of them and associated to viral infections in 4 others. The bacteria identified as single agents were: *Streptococcus pneumoniae* (2), *Haemophilus influenzae* (2), *Staphylococcus aureus* (2), *Salmonella arizonae* (1), *Mycobacterium tuberculosis* (1), Group B *Streptococcus* (1) e *Chlamydia trachomatis* (1). The four associations of viral agents with bacteria found were: RSV with *Streptococcus pneumoniae* (2); RSV and Adenovirus with *Neisseria meningitidis* (1), and RSV with gram-positive cocci, detected at pleural liquid bacterioscopy (1).

All children were provided outpatient follow-up care after discharge; there were no readmissions from Group A in the subsequent period of 15 days.

DISCUSSION

Our findings show that RSV is associated with severe LRD cases in infants and young children and that it practically does not occur in children admitted without respiratory pathologies (41.8% versus 1.7%) ($p < 0.0001$). Overall, the results regarding RSV were similar to those observed in different other countries, in accordance to the hypothesis that the virus is the single most frequent lower respiratory tract pathogen in infants and young children worldwide[4,16,41]. This conclusion assumes that RSV hospitalized LRD cases are only a part of those affected in the community as previously reported[1,2,4,17,20].

RSV significantly predominated over other viruses (100:14) and bacteria (100:15), indicating its leading role in the etiology of severe LRD in infants and young children in a developing country environment (Table 2). Although the results may be impressive, a few cautionary words should be said regarding these conclusions. During the study period, there were two RSV outbreaks within 18 months, a fact that increases the possibilities of finding this agent in the group of patients admitted for LRD (Fig. 1). This, however, does not invalidate the conclusion regarding the actual preponderance of RSV over other viruses. In the evaluation of one single year, from March 1995 to February 1996, the RSV was associated to 34 of the LRD cases, while just 9 were associated to other viruses, which is not different from the proportion found for the whole period ($p = 0.09$) (Fig. 1). In regard to the preponderance of RSV over bacteria as LRD pathogen in Group A, the analysis should be still be viewed with more caution. Along with other researchers, the authors have already concluded that most of the bacterial infections could only be recognized by pulmonary punction, a procedure that was not used in the study[22]. Additionally, the occurrence of mixed infections-virus/bacteria is a well known phenomenon, as was observed in 5 cases (5.0%) (Table 2), and that figure could be actually larger than the one detected[10, 11,14]. Another methodological aspect that can result in underestimation of the bacterial role in the present study involves the previous use of antibiotics, which occurred in 76 children (31.8%) from Group A (with LRD). The possibility of simultaneous occurrence of RSV infections with other respiratory pathogens, such as *Mycoplasma pneumoniae*, *Ureaplasma urealiticum*, *Pneumocystis carinii*, Cytomegalovirus, *Clamydia* sp, is infrequent[10,11,14]. The investigation of these agents, which was carried out for clinical reasons in some of the cases, could have increased the percentage of etiologic identification but probably did not affect the conclusions regarding the role of the RSV in the LRD cases studied.

Clinical patterns - Most of the children from Group A (with LRD) affected by RSV were small infants just a few months old, with a median age of 4.5 months (Table 2), as seen in other studies. The average age (4 months) of these children with RSV-LRD, was significantly lower than non-RSV-LRD children (11 months) from Group A ($p < 0.01$). The occurrence of RSV infections in the former months of life is due to the agent's impressive contagiousness, even in the presence of specific antibodies matternaly acquired[8].

In terms of the clinical and radiological aspects, most of the patients with RSV infections presented bronchial and/or alveolar involvement, and only few cases had an interstitial involvement, as already known[6,15,17] (Table 3). RSV infected patients have episodic bronchial/bronchiolar more frequently than isolated alveolar involvement or of recurrent bronchitis (Table 3). These data confirm that RSV is the main viral agent that causes acute bronchial pathologies, especially bronchiolitis[3]. Regarding the therapeutic aspects, we did not employ antiviral drugs, due to their doubtful efficacy[29]. When alveolar condensation was present, antibiotics were prescribed in the RSV-LRD cases, considering an eventual secondary bacterial infection[14].

Epidemiological aspects - The RSV seasonal occurrence is a recognized epidemiological aspect, which, however, is not uniform in all regions. In both years surveyed, there were two outbreaks beginning in late March or early April, peaking in May (fall season) that lasted for 5 months (Fig.1). This aspect observed in São Paulo City is similar to that verified in the City of Rio de Janeiro, also a region of subtropical climate. Seasonal RSV occurrence in temperate regions usually predominates in the winter, as seen in the United States and countries located in the southernmost regions of Latin America, such as Chile[2], Uruguay[35], and Argentina[43]. The peak of RSV outbreak in the autumn in São Paulo cannot be associated to the rainy seasons, which go from January through March and from September through November, nor to the coldest months, which go from June to August[23,31]. Conversely, the RSV peak coincides with the heavier levels of air pollution observed in the City of São Paulo. The association between environmental pollution and incidence of RSV has not been sufficiently assessed[23].

The parallel increase of ward admissions for LRD (Table 1) and RSV outbreaks (Fig.1) also highlights the major role of RSV in LRD. The higher indices of LRD hospitalization in May and June are associated with 68% of RSV occurrences (Fig. 1), although in April and July the RSV-related LRD cases were 35%. The RSV-LRD cases peak frequencies (85% in 1995 and 67% in 1996) were even higher than those observed in other countries (Chile 62%)[2,3,16]. If one observes simultaneously the RSV seasonality and the LRD patients' age bracket, the RSV cases affected 86% of infants under one year during the outbreak. The potential lethality of RSV was not observed in the present study in the 100 LRD cases in which it was detected. In regard to the mortality from LRD it is noteworthy to observe that there were no fatal cases among the 239 patients from Group A, but that 20 children died among the 597 non Group A LRD cases hospitalized in the same period (Table 1) ($p < 0.001$). Almost all these fatal cases, with the exception of three, were admitted directly to the intensive care unit from the time of their arrival to the hospital. We could hypothesize that, in our district, the LRD associated mortality is, possibly, justified by a late beginning of therapy more than by a given etiologic agent[32,36]. Even under this general observation, we did indirect evaluations to verify the possible link between RSV and the 20 LRD deaths observed during the period of the study. 13 from these fatal cases were registered during the 11 months of RSV outbreaks (Fig. 1). The monthly rate of deaths during this period (1.1 case/month) was similar to that seen in the other months (1.0 case/month) ($p = 0.765$). Another comparison shows the proportion of 13 fatal cases among 672 LRD children during the periods of RSV outbreak while 7 deaths were registered among 164 LRD cases in the remaining period of the year ($p = 0.14$) (Table 1 and Fig.1). These indirect evaluations, as the direct one, could not link the RSV infection and the LRD fatal evolution, as described previously[1]. Caution is advisable, since, conversely, the LRD mortality indicators for São Paulo State show a single death rate peak in late fall or winter (May and July) which parallels the RSV seasonality verified in our study[30]. Additionally, the São Paulo State LRD mortality peak is higher for children aged between 1 to 5 months, the most affected by RSV (Table 1)[30,41,43,44]. Thus, the role of RSV as an agent associated to fatal LRD cases should be better evaluated[28].

CONCLUSIONS

The RSV was the most important virus and a frequent pathogen associated to severe LRD, especially for socioeconomically deprived infants, in São Paulo, Brazil. The RSV yearly outbreak occurred in the fall extending to the winter, as observed in subtropical climate regions, and it parallels an increase in LRD hospitalization rate, in a pattern similar to what occurs in the Northern Hemisphere. No specific therapeutic measures were adopted, but, in regard to survival, the evolution of all cases was favorable. Also, RSV outbreaks did not change the nosocomial LRD mortality rate. In view of the frequency of severe cases due to RSV, prophylactic measures should be considered, particularly for infants with lung malformations and for prematures[34]. The development of vaccines for RSV should take into account the very young age of the affected children, and, thus, the emphasis should be placed on developing products that are suitable for use in newborns and pregnant women.

RESUMO

Padrões clínicos e sazonalidade das hospitalizações causadas pelo vírus respiratório sincicial em São Paulo, Brasil

Os vírus respiratórios são reconhecidos como os mais frequentes patógenos do trato respiratório inferior para lactentes e crianças de idade reduzida em países desenvolvidos, mas o conhecimento sobre este fato é menor nos países em desenvolvimento.Os autores realizaram um estudo prospectivo para avaliar a ocorrência, os padrões clínicos e a sazonalidade das infecções virais entre as crianças hospitalizadas com doença do trato respiratório inferior (grupo A). A presença de vírus respiratórios na nasofaringe das crianças foi avaliada à admissão em uma enfermaria de pediatria. A cultura celular e a imunofluorescência foram utilizadas para identificação viral. Exames complementares incluiram culturas de sangue e líquido pleural para detecção de bactérias. Dados clínicos e exames radiológicos foram anotados na admissão e durante o período de internação. Para avaliar adequadamente os resultados foi constituído um grupo sem doença respiratória para comparação. Com início em fevereiro de 1995, durante um período de 18 meses, 414 crianças foram incluídas - 239 no grupo A e 175 no grupo B. No grupo A, 111 crianças (46,4%) tinham vírus enquanto somente 5 (2,9%) apresentavam vírus no grupo B. O Vírus Respiratório Sincicial foi detectado em 100 crianças do grupo A (41,8%), o Adenovírus em 11 (4,6%), o vírus Influenza em 2 (0,8%), e o Parainfluenza em uma criança (0,4%). No grupo A as bactérias foram encontradas em 14 casos (5,8%). O Vírus Respiratório Sincicial estava associado a outro vírus ou bactéria em seis casos. Ocorreram dois surtos de Vírus Respiratório Sincicial, com pico em maio e junho. Todas as crianças acometidas por este vírus tinham idade inferior a 3 anos, na sua maior parte menos de um ano de idade. O acometimento bronquial episódico e difuso e/ou a condensação alveolar focal, foram os padrões clínicos mais frequentemente associados aos casos de infecção pelo Vírus Respiratório Sincicial. Todas as crianças do grupo A sobreviveram. Em

conclusão, foi observado que o Vírus Respiratório Sincicial foi o patógeno mais frequentemente encontrado em crianças hospitalizadas por doença respiratória grave. As crianças afetadas eram predominantemente lactentes do sexo masculino com bronquiolite e pneumonias focais. De modo similar ao que ocorre em outras regiões subtropicais os surtos do vírus têm pico no outono, extendem-se ao inverno, e se acompanham de um aumento nas internações hospitalares por doença respiratória.

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