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ORIGINAL ARTICLE

Seasonal patterns of viral and bacterial infections among children hospitalized with community-acquired pneumonia in a tropical region

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Abstract

Community-acquired pneumonia (CAP) is a common cause of morbidity among children. Evidence on seasonality, especially on the frequency of viral and bacterial causative agents is scarce; such information may be useful in an era of changing climate conditions worldwide. To analyze the frequency of distinct infections, meteorological indicators and seasons in children hospitalized for CAP in Salvador, Brazil, nasopharyngeal aspirate and blood were collected from 184 patients aged <5 y over a 21-month period. Fourteen microbes were investigated and 144 (78%) cases had the aetiology established. Significant differences were found in air temperature between spring and summer ($p = 0.02$) or winter ($p < 0.001$), summer and fall ($p = 0.007$) or winter ($p < 0.001$), fall and winter ($p = 0.002$), and on precipitation between spring and fall ($p = 0.01$). Correlations were found between: overall viral infections and relative humidity ($p = 0.006$; $r = 0.6$) or precipitation ($p = 0.03$; $r = 0.5$), parainfluenza and precipitation ($p = 0.02$; $r = -0.5$), respiratory syncytial virus (RSV) and air temperature ($p = 0.048$; $r = -0.4$) or precipitation ($p = 0.045$; $r = 0.4$), adenovirus and precipitation ($p = 0.02$; $r = 0.5$), pneumococcus and air temperature ($p = 0.04$; $r = -0.4$), and Chlamydia trachomatis and relative humidity ($p = 0.02$; $r = -0.5$). The frequency of parainfluenza infection was highest during spring (32.1%; $p = 0.005$) and that of RSV infection was highest in the fall (36.4%; $p < 0.001$). Correlations at regular strength were found between several microbes and meteorological indicators. Parainfluenza and RSV presented marked seasonal patterns.

Introduction

Community-acquired pneumonia (CAP) is a common cause of morbidity among children, mostly in those aged under 5 y, imposing a heavy burden on health care systems [1]. Currently, about 20% of the overall child mortality burden is attributable to CAP disease, of which 95% occurs in developing countries [2]. The clinical presentation is similar for CAP caused by different agents, but the epidemiological impact differs among several causative microbes [3]. Nonetheless, data on specific aetiological agents are scarce, especially from developing countries, because of a lack of means to accurately establish the aetiology [4]. Evidence on seasonality, particularly on the frequency of viral and bacterial causative agents is scarce; such information may be useful in an era of changing climate conditions worldwide.

We aimed to describe the frequency of bacterial and viral infections among children hospitalized for CAP in a tropical region across the seasons of the y, analyzing the association between the different aetiological agents and meteorological indicators.

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Methods

Study setting and participants

This is a subsequent analysis of data collected during a prospective study conducted at the Professor Hosannah de Oliveira Paediatric Centre, Federal University of Bahia, Salvador, in the northeast of Brazil, from September 2003 to May 2005. The latitude and the longitude of Salvador are 12° 53′ 48″ and 38° 31′ 36″, respectively [5].

Patients with respiratory complaints and fever, or difficulty in breathing, had a chest radiograph (CXR) performed at admission. The inclusion criteria included age <5 y and radiologically diagnosed pneumonia defined as the presence of a pulmonary infiltrate. A second CXR (2–4 weeks after recruitment) was taken to confirm resolution of pneumonia. A paediatric radiologist blind to clinical information read both CXR.

Initially, 322 consecutive patients were evaluated. Exclusion was due to: refusal to give informed consent ($n = 28$), child born to an HIV-infected woman ($n = 6$), chronic lung disease except asthma ($n = 6$), varicella ($n = 3$), and immunodeficiency ($n = 2$). Pneumonia was confirmed by the paediatric radiologist in 206 patients, of whom 184 had radiological resolution documented; these 184 comprised the study group, assuring the acute course of the studied CAP cases.

The study protocol was approved by the Ethics Committee of the Federal University of Bahia and by the Brazilian National Research Ethics Committee. Informed consent was obtained before enrolment.

Biological samples

On admission, a blood sample was collected for serologic analysis, reverse transcription-polymerase chain reaction (RT-PCR) search and blood culture; a nasopharyngeal sample was aspirated through a nostril and kept at −70°C until virological tests. A clinical examination was carried out 2–4 weeks after admission, when the second blood sample for serologic tests was taken.

Viral antigens (influenza A and B viruses, respiratory syncytial virus (RSV), parainfluenza virus types 1, 2, and 3, and adenovirus) in nasopharyngeal aspirates were searched for using a time-resolved fluoroimmunoassay with monoclonal antibodies [6]. Virus-specific serum antibody titres were determined using an enzyme-immunoassay (EIA) [6]. A PCR assay was used for the detection of rhinoviruses [7]. The virological studies were carried out in Turku, Finland.

Antibodies against Streptococcus pneumoniae, non-typable Haemophilus influenzae and Moraxella catarrhalis were measured using an in-house EIA [8]. Chlamydia trachomatis IgG antibodies were detected using a commercial, solid-phase EIA [9]. PCR was used for the detection of S. pneumoniae DNA in blood buffy-coat [10] after extraction of DNA. These bacterial tests were done in Oulu, Finland. IgM antibodies to Mycoplasma pneumoniae were searched for using a commercial EIA kit [11] in Salvador, Brazil.

Meteorological data

Data on air temperature, relative humidity and precipitation were collected from the Institute of Water Monitoring in the State of Bahia, Brazil (INGA) [5]. Data on air temperature and relative humidity were registered every 3 h, daily and on precipitation were registered once a day. For the purposes of the analysis performed in this study, the month average of air temperature and relative humidity as well as the total precipitation during each month were calculated. The seasons and correspondent months were defined as follows: summer (January, February, March), fall (April, May, June), winter (July, August, September) and spring (October, November, December).

Data analysis

The distribution of viral, bacterial and any potential pathogen was depicted according to the season. Correlation between the meteorological indicators and the frequency of the aetiologies was assessed by the Pearson or Spearman test, as appropriate. The Pearson Chi-square test was used to compare the proportions among the age groups. The distribution of continuous variables among 4 groups was compared by 1-way analysis of variance (ANOVA) and the groups with significant differences were identified by Turkey. SPSS and STATA (both version 9.0) packages were used for data analysis. The analysis of the frequency of the aetiological agents according to age distribution has been published [12].

Results

There were 109 (59%) boys and 75 (41%) girls, all of them previously healthy. Their median age was 1.6 y (range 26 days–4.9 y). An aetiological agent was found in 144 (78%) of the 184 cases, out of which 43 (23%) were bacterial–viral. Nine viruses were searched for and found at the following frequencies: rhinovirus (21%), parainfluenza viruses (17%), RSV (15%), influenza A and B viruses (9%), enterovirus (5%), adenovirus (3%). The detected bacterial pathogens were S. pneumoniae (21%), H. influenzae (8%),

Table I. Meteorological indicators in Salvador, northeast Brazil, during the study on the aetiology of community-acquired pneumonia in hospitalized children.

Y	Index	Month											
		Jan	Feb	Mar	Apr	May	Jun	Jul	Aug	Sep	Oct	Nov	Dec
2003	Air temperature (°C)[a]	-	-	-	-	-	-	-	-	24.4	25.3	26.0	25.6
	Relative humidity (%)[a]	-	-	-	-	-	-	-	-	88.0	85.1	89.3	91.8
	Total precipitation (mm)	-	-	-	-	-	-	-	-	152.75	97.75	59.5	0
2004	Air temperature (°C)[a]	26.5	26.9	26.9	26.5	25.5	24.5	23.7	23.3	24.6	25.5	26.1	26.7
	Relative humidity (%)[a]	90.0	87.3	88.8	89.8	92.0	93.4	88.4	93.3	86.6	89.8	89.9	88.9
	Total precipitation (mm)	344.0	123.5	51.25	238.5	139.75	275.75	166.0	167.75	28.25	28.25	239.5	0.25
2005	Air temperature (°C)[a]	27.0	26.7	27.2	26.1	25.5	-	-	-	-	-	-	-
	Relative humidity (%)[a]	91.8	96.4	95.1	96.0	96.8	-	-	-	-	-	-	-
	Total precipitation (mm)	140.5	258.0	251.0	390.5	307.25	-	-	-	-	-	-	-

[a]Results are monthly average.

M. pneumoniae (8%), C. trachomatis (4%), and M. catarrhalis (3%).

During the study period, the median of the month average of relative humidity, air temperature and of total month precipitation were 90% (mean 91% ± 3%, minimum 85%, maximum 97%), 26.0°C (mean 26°C ± 1°C, minimum 23.3°C, maximum 27.2°C) and 152 mm (mean 165 ± 115 mm, minimum 0 mm, maximum 390 mm), respectively. Table I presents the meteorological indicators per month during the study period and Table II presents the comparison of the meteorological indicators among seasons. Significant differences were found in air temperature between spring (October, November, December) and summer (January, February, March) ($p = 0.02$), spring (October, November, December) and winter (July, August, September) ($p < 0.001$), summer (January, February, March) and fall (April, May, June) ($p = 0.007$), summer (January, February, March) and winter (July, August, September) ($p < 0.001$), and fall (April, May, June) and winter (July, August, September) ($p = 0.002$) and in precipitation between spring (October, November, December) and fall (April, May, June) ($p = 0.01$). Fall is the rainy season. Overall, 34 (18.5%), 55 (29.9%), 39 (21.2%) and 56 (30.4%) CAP cases occurred during the summer (January, February, March), fall (April, May, June), winter (July, August, September) and spring (October, November, December), respectively, and the frequency of detected aetiology was similar between these seasons (76%, 84%, 77%, 75%, $p = 0.7$).

Table III presents the distribution of the monthly frequency of the infections detected according to the aetiology established. Table IV shows the assessment

Table II. Comparison of meteorological indicators among seasons during the study on the aetiology of community-acquired pneumonia in hospitalized children, in Salvador, northeast Brazil.

Seasons (number of months included)[a]	Meteorological indicators: Average relative humidity (%)	Average air temperature (°C)	Total precipitation (mm)
Spring (n = 6)			
Mean ± SD	89.1 ± 2.2	25.9 ± 0.5	70.9 ± 90.7
Median	89.6	25.8	43.9
Minimum, maximum	85.1–91.8	25.3–26.7	0–239.5
Summer (n = 6)			
Mean ± SD	91.6 ± 3.6	26.9 ± 0.2	194.7 ± 107.8
Median	90.9	26.9	195.8
Minimum, maximum	87.3–96.4	26.5–27.2	51.2–344.0
Fall (n = 5)			
Mean ± SD	93.6 ± 2.9	25.6 ± 0.8	270.4 ± 92.1
Median	93.4	25.5	275.75
Minimum, maximum	89.8–96.8	24.5–26.5	139.75–390.5
Winter (n = 4)			
Mean ± SD	89.1 ± 2.9	24.0 ± 0.6	128.7 ± 67.3
Median	88.2	24.0	159.4
Minimum, maximum	86.6–93.3	23.3–24.6	28.2–167.8
p-Value	0.08	<0.001	0.02

[a]Summer: January, February, March; fall: April, May, June; winter: July, August, September; spring: October, November, December.

Table III. The distribution of the monthly frequency of infections according to the aetiology detected among hospitalized children with community-acquired pneumonia.

Aetiology	No. of months	Frequency (%) per month among CAP cases			
		Mean ± SD	Median	Minimum	Maximum
Viral infection	21	61 ± 15	60	38	100
Rhinovirus	17	20 ± 15	18	0	50
Parainfluenza 1, 2, 3	14	17 ± 18	17	0	50
RSV	9	13 ± 18	0	0	54
Influenza A, B	9	11 ± 23	0	0	100
Enterovirus	7	4 ± 7	0	0	25
Adenovirus	6	5 ± 12	0	0	50
Bacterial infection	20	44 ± 22	46	0	100
Streptococcus pneumoniae	17	20 ± 15	20	0	60
Haemophilus influenzae	10	6 ± 8	0	0	25
Mycoplasma pneumoniae	12	12 ± 22	7	0	100
Chlamydia trachomatis	7	6 ± 12	0	0	50
Moraxella catarrhalis	5	3 ± 7	0	0	25

RSV, respiratory syncytial virus.

of correlation between the meteorological indicators and the infections caused by different aetiological agents. Table V presents the frequency of each aetiological agent per season with the respective statistical analysis. The significant difference for RSV infection was maintained on stratified analysis for age groups (<1 y, ≥1 y, <2 y, ≥2 y) (data not shown). The difference for infection with parainfluenza viruses was significant only for the age group ≥2 y (data not shown).

Discussion

Marked seasonal patterns of RSV and parainfluenza virus infection are reported in this study. RSV has been recognized as the one of the most frequent aetiological agents responsible for hospitalization in young children, across the globe [13]. In temperate climates, RSV usually occurs during winter (July, August, September) and early spring (October, November, December) [14]. Nonetheless, in Salvador, a tropical city situated in the lower northeast of Brazil, RSV infection peaked in the fall (April, May, June) (Table V). This finding is in accordance with the results of a previous study where children with acute respiratory infection were investigated in Salvador [15] and a recently conducted study in São Paulo, a subtropical city in Brazil [16]. A possible explanation is the circulation of RSV from temperate to tropical regions, during the spring (October,

Table IV. Assessment of correlation between the meteorological indicators and the infections caused by different aetiological agents among children hospitalized with community-acquired pneumonia.

Aetiology	Meteorological indicators per month		
	Average relative humidity	Average air temperature	Total precipitation
Viral infection[a]	0.006[c] (0.6)	0.7	0.03 (0.5)
Rhinovirus[a]	0.05	0.6	0.6
Parainfluenza 1, 2, 3[a]	0.4	0.8	0.02 (−0.5)
RSV[b]	0.2	0.048 (−0.4)	0.045 (0.4)
Influenza A, B[b]	0.3	0.6	0.8
Enterovirus[b]	0.3	0.6	0.3
Adenovirus[b]	0.1	0.6	0.02 (0.5)
Bacterial infection[a]	0.3	0.7	0.8
Streptococcus pneumoniae[a]	0.6	0.04 (−0.4)	0.7
Haemophilus influenzae[b]	0.9	0.6	0.4
Mycoplasma pneumoniae[b]	0.06	0.3	0.09
Chlamydia trachomatis[b]	0.01 (−0.5)	0.3	0.3
Moraxella catarrhalis[b]	0.6	0.9	0.6

Results are p-values (r in parenthesis when p is significant). RSV, respiratory syncytial virus.
[a]Pearson correlation.
[b]Spearman correlation.
[c]Significance at 0.01 level.

Table V. The frequency of different aetiological agents among hospitalized children with community-acquired pneumonia per season.

	Seasons[a]				
Aetiology	Spring (n = 56)	Summer (n = 34)	Fall (n = 55)	Winter (n = 39)	p-Value
Viral infection	29 (51.8)	21 (61.8)	37 (67.3)	24 (61.5)	0.4
Rhinovirus	9 (16.1)	7 (20.6)	9 (16.4)	13 (33.3)	0.2
Parainfluenza 1, 2, 3	18 (32.1)	4 (11.8)	4 (7.3)	6 (15.4)	0.005
RSV	0	1 (2.9)	20 (36.4)	7 (17.9)	<0.001
Influenza A, B	4 (7.1)	7 (20.6)	5 (9.1)	1 (2.6)	0.06
Enterovirus	4 (7.1)	1 (2.9)	5 (9.1)	0	0.09
Adenovirus	0	2 (5.9)	3 (5.5)	1 (2.6)	0.2
Bacterial infection	25 (44.6)	11 (32.4)	25 (45.5)	16 (41.0)	0.6
Streptococcus pneumoniae	15 (26.8)	4 (11.8)	11 (20.0)	9 (23.1)	0.4
Haemophilus influenzae	4 (7.3)	3 (9.1)	6 (10.9)	2 (5.6)	0.8
Mycoplasma pneumoniae	3 (5.4)	2 (5.9)	6 (10.9)	3 (7.7)	0.7
Chlamydia trachomatis	3 (5.4)	1 (2.9)	2 (3.6)	3 (7.7)	0.8
Moraxella catarrhalis	2 (3.6)	0	2 (3.6)	1 (2.8)	0.5

Results are n (%). RSV, respiratory syncytial virus.
[a]Summer: January, February, March; fall: April, May, June; winter: July, August, September; spring: October, November, December.

November, December) (in temperate regions) and fall (April, May, June) (in tropical regions) since they occur concomitantly. The RSV season in Fortaleza, a city in the upper northeast of Brazil, was described to start in the summer (January, February, March) and finish in the winter (July, August, September) [17]. The RSV season is broader in Fortaleza than in Salvador or São Paulo and regional differences should be noticed. A humanized mouse (anti-RSV) monoclonal immune globulin (palivizumab) is recommended as prophylaxis for some high-risk children [18]. Palivizumab must be administered at the beginning of and throughout the RSV season to be effective [18]. Therefore, the recognition of the seasonal pattern of RSV infection in this tropical region is of paramount importance to guide the timing of palivizumab use.

Parainfluenza virus infections peaked in spring (October, November, December) (Table V) among children aged ≥2 y. The frequency of parainfluenza infection is greatest in preschool-age children [19], and outbreaks usually occur during the fall–winter in temperate climate countries [20]. The marked seasonality observed in parainfluenza infection among toddlers and older children is attributable to the age predominance of this infection. The peak in occurrence during the spring (October, November, December) may be due to the rapid circulation of these viruses because of the great influx of travellers from temperate countries to Salvador during the vacation season. Several respiratory virus epidemics have been described to occur when religious festivals bring large numbers of people into the same area [20]. A similar process occurs in Salvador. Parainfluenza virus has been shown to cause outbreaks in the subtropical city of Rio de Janeiro annually during the late winter (July, August, September) and spring (October, November, December) [21]. This discrepancy reinforces the necessity of continuous surveillance for respiratory virus infections in large regions.

Rhinovirus, the most commonly detected virus, occurred endemically all y round, peaking in the winter (July, August, September), but without statistical significance (Table V). There is scarce information on the epidemiology of rhinovirus in our country. A previous longitudinal study did not find seasonal predominance of this infection [21] and this report is in accordance with our results. Caution must be taken in interpreting data on rhinovirus infection because of the molecular cross-reactions in the detection of enterovirus and rhinovirus. Nonetheless, we used the more sensitive RT-PCR assay for this diagnosis [7].

Interestingly, despite being a tropical region where variations are narrow in the meteorological indicators, differences were found between the seasons, especially in air temperature (Table II). An inverse correlation could be observed between pneumococcal infections and air temperature (Table IV), i.e., the lower the temperature, the higher the frequency of pneumococcal infection. The wintertime predominance of invasive pneumococcal disease (IPD) has recently been published, being described in Philadelphia, a temperate region where extended periods of low UV radiation were identified as a major predictor of IPD [22]. A population-based study in Taiwan demonstrated that a 1°C decrease in ambient temperature was associated with a 0.03 increase in monthly CAP hospitalization [23]. In the latter study, aetiology was not investigated. Nonetheless, as S. pneumoniae is the most common bacterial cause of CAP, it is possible to infer that the association between decreased air temperature and increased CAP hospitalization rate was due to the inverse correlation reported herein.

We collected data over a 21-month period with an under-representation of 1 fall month (June) and of 2 winter months (July, August); this is a limitation in our study since some viral infections may switch from an early epidemic peak one y to a late one in the next. Nonetheless, the analysis of the frequencies of infection and the meteorological indicators on a monthly basis overcome this. The correlations found were at regular strength (r 0.3–0.6), which may be attributable to the typical narrow variations in the meteorological indicators in a tropical region.

We provide evidence that even narrow variations in climatic conditions are correlated with the frequencies of distinct causative agents of CAP. This information should be taken into account in the discussions and decision-making regarding the climate in the world.

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