
Effect of climatological factors on respiratory syncytial virus epidemics

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SUMMARY

Respiratory syncytial virus (RSV) presents as yearly epidemics in temperate climates. We analysed the association of atmospheric conditions to RSV epidemics in San Luis Potosí, S.L.P., Mexico. The weekly number of RSV detections between October 2002 and May 2006 were correlated to ambient temperature, barometric pressure, relative humidity, vapour tension, dew point, precipitation, and hours of light using time-series and regression analyses. Of the variation in RSV cases, 49·8% was explained by the study variables. Of the explained variation in RSV cases, 32·5% was explained by the study week and 17·3% was explained by meteorological variables (average daily temperature, maximum daily temperature, temperature at 08:00 hours, and relative humidity at 08:00 hours). We concluded that atmospheric conditions, particularly temperature, partly explain the year to year variability in RSV activity. Identification of additional factors that affect RSV seasonality may help develop a model to predict the onset of RSV epidemics.

INTRODUCTION

Acute respiratory infections are a leading cause for medical visits and hospitalizations in children worldwide [1]. Respiratory syncytial virus (RSV) is the leading cause for lower respiratory tract infections (LRTI) and hospitalizations in young children [2, 3]. In temperate climates RSV infections present as yearly epidemics, starting in autumn and ending in spring. However, the onset of each epidemic may vary not only from year to year but also in different regions [4, 5]. It has not been clearly defined which factors determine the variation in the onset of RSV infections in a community but several studies have found that environmental factors are associated with RSV

activity in the community [6–8]. Ambient temperature has been inversely associated with RSV activity, although the highest number of cases does not necessarily coincide with the lowest temperature [6–8]. In some areas of the world, such as Hong Kong, RSV epidemics are more frequent during the rainy season, when the temperature is hot [9]. The determination of seasonal RSV activity in different areas of the world is important because current preventive strategies for RSV infections in high-risk populations rely on the administration of monoclonal antibodies during the months when RSV is most frequent in a community. Currently, the months when palivizumab needs to be administered depends on virological surveillance data. If the start of the RSV season is proven to depend on climatological changes, then it is possible that the beginning of the season could be predicted. This information could be helpful in areas where continued viral surveillance is not available. To assess this issue we studied the role of atmospheric conditions in the

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city of San Luis Potosí, S.L.P., Mexico and their relation to RSV epidemiology during four consecutive epidemics.

METHODS

The city of San Luis Potosí is located in central Mexico at 100° 58' 34" longitude, 22° 9' 4" latitude, and an elevation of 1860 m above sea level [10]. The average annual temperature varies from 16 °C to 18 °C and the maximums are registered in May and June with 21.7 °C and 22 °C respectively and the minimum in January with 13.6 °C. The temperature falls below freezing between 5 and 10 days per year. Precipitation varies between 336 mm and 396 mm per year and is most abundant in the month of September with 69.3 mm and is lowest in January with 5.3 mm.

Detection of RSV activity

We reviewed the records of the virology laboratory at the Facultad de Medicina, Universidad Autónoma de San Luis Potosí (UASLP) and determined the weekly number of RSV positive samples from children admitted with LRTI to the Hospital Central 'Dr. Ignacio Morones Prieto' which is a public general hospital that provides acute and speciality care in the city of San Luis Potosí. The study included the period between October 2002 and May 2006. Since October 2002 all children admitted with LRTI have been screened to detect the presence of RSV by the use of a direct fluorescence antibody assay as previously described [11]. Viral detection was performed initially as part of a research project to determine the contribution of respiratory viruses to LRTI [11, 12]. Currently, viral screening is performed as part of the hospital's infection control programme.

Meteorological data

Meteorological data for the city of San Luis Potosí was obtained from the Laboratorio de Meteorología, Área Agrogeodésica, Facultad de Ingeniería, UASLP. The data was reviewed, corrected, and captured in Excel and missing data (2657 values or 14.17% of the 18 746 cell data matrix) were estimated using multiple imputation [13] with R version 2.3.1 [14] using the daily readings for minimum temperature, maximum temperature, precipitation, and hours light, and the following readings at 08:00, 12:00, and 18:00 hours: temperature, barometric pressure, relative humidity,

vapour tension, and dew point. The average daily temperature was calculated and weekly averages were calculated to coincide with the RSV data.

Statistical analysis

Regression analysis, which describes the dependence of a response variable on one or more explanatory variables and which assumes that there is a one-way causal effect from the explanatory variables to the response variable, was used rather than correlation analysis, which makes no *a priori* assumption as to whether one variable is dependent on the others or not and is not concerned with the relationship between variables but rather estimates the degree of association between the variables. Both the predicted and the observed values are utilized in the analysis as the predicted values for the model are compared with the observed values to evaluate the adequacy of the model.

The number of RSV positive cases was modelled in two stages. First, a polynomial was fitted for study week using likelihood ratio tests. Second, the meteorological variables were added linearly following the procedure recommended by Harrell [15] of excluding non-significant variables [16]. In the final model, outliers as defined by Tukey were identified (nine or 4.762%), examined, and maintained. Influential repetitions were identified (18 or 9.52%). Residuals were tested for normality with the Shapiro-Wilk procedure, $P < 0.0001$ indicating no normality. The skew coefficient of 1.731 indicated positive skew. Variance homogeneity was evaluated graphically. Collinearity was evaluated with the variance inflation factors (VIF) which with the exception of the polynomial terms, the data were not centred, were < 7 and acceptable.

RESULTS

The virological surveillance data included in this study encompassed four RSV epidemic seasons. RSV was detected in 368 (26.4%) of 1393 samples from children with LRTI obtained during the study period.

The best fit was a sixth-degree polynomial and it should be noted that forecasts are often poor with high-degree polynomials [17]. Average daily temperature, maximum daily temperature, temperature at 08:00 hours, and relative humidity at 08:00 hours also were included in the final model which had an *F* value calculated of 17.7 with 10 D.F. and 178 D.F.

Table. Meteorological conditions associated with the weekly number of respiratory syncytial virus detections

Term	Regression coefficient	Lower confidence limit	Upper confidence limit	η^2	F value	P
Intercept	12.6	7.831	17.41			
Week ¹	-0.56	-1.06	-0.067	0.008	2.91	0.089
Week ²	0.012	-0.0076	0.032	0.050	17.89	<0.0001
Week ³	-8.80×10^{-5}	-4.56×10^{-4}	2.79×10^{-4}	0.029	10.17	0.0017
Week ⁴	-2.59×10^{-7}	-3.63×10^{-6}	3.113×10^{-6}	0.046	16.31	<0.0001
Week ⁵	5.10×10^{-9}	-9.85×10^{-9}	2.00×10^{-8}	0.164	58.18	<0.0001
Week ⁶	-1.43×10^{-11}	-3.98×10^{-11}	1.12×10^{-11}	0.028	9.85	0.002
Mean temperature	-0.297	-0.667	0.073	0.102	36.18	<0.0001
Maximum temperature	0.25	0.08	0.43	0.021	2.88	0.0067
Temperature at 08:00 hours	-0.36	-0.62	-0.094	0.023	2.68	0.0045
Relative humidity at 08:00 hours	0.035	0.012	0.058	0.026	3.04	0.0027

and $P < 0.0001$ (Table). The weekly number of observed and predicted RSV cases are shown in the Figure. Of the variation in RSV, 49.8% was explained by the model and 50.2% of the variation was not explained. The correlation ratios (η^2), which represent the proportion of the total variability in RSV activity explained by each of the explanatory variables, are presented in the Table. The regression terms related to study week explain 32.5% and the climatic conditions explain 17.3% of the total variation in RSV.

DISCUSSION

We found that climatological factors are significantly associated with RSV activity in San Luis Potosí. Average weekly temperature was inversely correlated to RSV activity and was the most important climatological feature associated with RSV variations. This observation is similar to that reported in other areas of the world [6–8, 18, 19]. In contrast, some authors have reported that RSV outbreaks in tropical or subtropical areas may occur during the hot, rainy season [9]. However, in a study performed in Sao Paulo, Brazil, the peak of RSV activity was observed in autumn and RSV activity was not associated with the rainy season [20]. We observed a negative association between RSV infections, mean weekly temperature, and temperature at 08:00 hours. There was a positive association between mean maximal temperature and the number of RSV cases when all other variables are constant. A higher maximal temperature would indicate a greater fluctuation in daily temperature which may explain this observation. In addition to temperature, we observed that ambient humidity affects RSV activity. Lapeña and colleagues

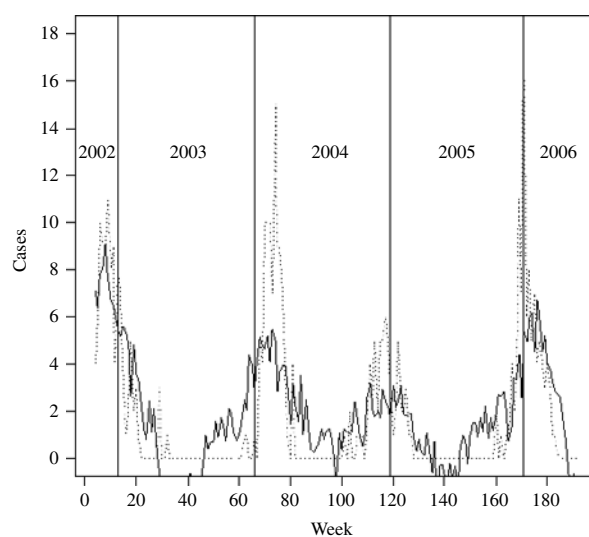


Fig. Weekly number of observed (·····) and predicted (—) respiratory syncytial virus cases.

also reported that decreased ambient relative humidity was associated with increased hospital admissions caused by RSV in Spain [21]. Recently, Donaldson reported a shortening in RSV epidemics during recent years in England, correlated with an increase in average annual temperature [22]. This observation also supports the notion that climate influences RSV epidemiology.

Seasonal variations in the appearance of many infectious diseases have been reported [23]. Invasive pneumococcal disease presents with seasonal patterns that are related to temperature fluctuations [24–26]. Photoperiod has also been associated with invasive pneumococcal disease [25]. We did not find any association between photoperiod and RSV activity.

In addition to the effect of climatic conditions, the effect of latitude on the epidemic pattern of RSV

infections has been reported. In cities located within 19·2° to 25·8° N latitude (Mexico City and Miami), RSV activity was present throughout the year peaking during late summer and autumn [27]. In San Luis Potosí, located at 22·15° N, RSV activity showed a clear epidemic pattern with peak activity during autumn or winter. This pattern (autumn and winter RSV epidemics with no activity during the hot months) resembles more closely the patterns observed in Tucson (located at 32·1° N latitude) and other locations where climate is dry and hot during summer.

We did not include air pollution as one of the possible factors influencing RSV activity in our study as we did not have such data available. However, Avendaño *et al.* and Zamorano *et al.* have studied the effect of air pollution on RSV epidemiology and did not find any association between air pollutants and RSV epidemiology [28, 29].

Several hypotheses have been used to explain the seasonality of infectious diseases, including the introduction and disappearance of a pathogen in a community, environmental changes, and changes in host behaviour or susceptibility [23]. The development of immunity to an infectious agent certainly impacts the epidemiology of the disease it causes as can be seen after the introduction of vaccines in a population. Mathematical models that take into account immunity development and simulate transient decrease in transmissibility can produce epidemic curves that fit observed RSV epidemics closely [30]. The effects of climate on viral transmissibility or on host susceptibility to infection are possible explanations for the association between atmospheric conditions and RSV epidemics. Ultraviolet B (UVB) radiation is an environmental factor that has seasonal fluctuations and has been shown to correlate with RSV infections [31]. UVB radiation measurements in San Luis Potosí are greater between March and August [32], the months when the lowest or no RSV activity was detected in our study. Lower UVB radiation during winter is associated with low vitamin D levels, particularly in infants that do not receive vitamin supplementation [33]. Low levels of vitamin D have been associated with increased susceptibility to respiratory tract infections in children [34]. This association may be explained by the modulating effect of vitamin D on the immune system. Vitamin D up-regulates the expression of antimicrobial peptides [35–37]. These molecules participate in the innate immune response in the respiratory tract and can inactivate some viruses and other respiratory pathogens [38, 39]. Conduction

of studies that measure vitamin D levels coupled with vitamin D supplementation programmes for infants during winter would be helpful to determine the possible preventive effect of vitamin D on respiratory infections in young children.

A practical implication for clarification of these issues would be the ability for accurate prediction of the onset of yearly RSV and other yearly viral epidemics. Although almost half of the variability of RSV activity could be accounted for by variables included in this study, there are other important factors that could not be identified. Therefore, accurate prediction of RSV outbreaks using temperature and ambient humidity information is not possible at this time. Identification of additional factors that may be involved in triggering RSV epidemics in a community may be of help for prediction purposes and could constitute targets for preventive strategies.

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DECLARATION OF INTEREST

None.

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