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The importance of the local environment in the transmission of respiratory syncytial virus☆,☆☆

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HIGHLIGHTS

- Many environmental exposures can influence the transmission of respiratory infections.
- Nutrition is a plausible driver of RSV seasonality in the Gambia.
- Rainfall is a plausible driver of RSV seasonality in Southeast Florida.
- Understanding how the environment affects transmission can improve RSV control.

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ABSTRACT

The role of the environment in the spread of respiratory infections is poorly understood, and consequently probably underappreciated. To improve our understanding of the environmental drivers of respiratory syncytial virus (RSV) transmission, we examined RSV seasonality in two settings with unusual seasonal patterns: The Gambia (where RSV epidemics occur at different times of the year) and Southeast Florida (where RSV seasonality differs from the rest of mainland USA). We used published data to correlate the seasonality of RSV with rainfall and child nutrition in the Gambia, and with rainfall and temperature in Florida. In the Gambia, RSV incidence was more strongly and more consistently correlated with child nutrition ($r = -0.73$ [95%CI −0.90 to −0.38]) than with rainfall ($r = 0.37$ [95%CI 0.20 to 0.52]). In Southeast Florida RSV incidence was strongly correlated with rainfall two months previously ($r = 0.65$ [95%CI 0.40 to 0.81]) compared to North Florida where RSV incidence was strongly correlated with temperature ($r = -0.75$ [95%CI −0.87 to −0.56]). We propose that nutrition is the dominant environmental driver of RSV seasonality in the Gambia, while rainfall is the dominant driver of RSV seasonality in Southeast Florida. This reinforces the importance of an ecological scale understanding of disease transmission: only with such an evidence base can setting-specific recommendations be made for public health interventions that are targeted for maximum efficacy.

1. Introduction

The role of the environment in the spread of respiratory infections is poorly understood, and consequently probably underappreciated. The seasonal patterns seen for almost all respiratory infections are one of the more evident manifestations of the effects of the environment on transmission. Respiratory syncytial virus (RSV) is a viral respiratory infection, responsible for approximately seven percent of deaths in infants globally, with most deaths occurring in tropical settings (Lozano et al., 2012). RSV incidence is typified by marked seasonal epidemics. Environmental forcing of RSV transmission is required to maintain this seasonality, and to dictate the timing of seasonal epidemics (White et al., 2007). In tropical settings seasonal RSV epidemics generally occur during the rainy season, however there are several exceptions to this rule (Weber et al., 1998; Tang and Loh, 2014; Robertson et al., 2004). A number of environmental drivers have been hypothesised to explain the tendency for RSV epidemics to occur during tropical rainy seasons. It is thought that during tropical rainy seasons time spent indoors may be increased, resulting in increased opportunity for transmission (Murray et al., 2012; Tang and Loh, 2014). Variations in humidity may affect RSV survival in the environment (Hambling, 1964; Kingston, 1968). In equatorial regions rainy seasons are also a time of reduced

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sunshine (cloud cover being a more important determinant of sunshine levels than day length in equatorial latitudes) which may impact on child immunity as well as on viral survival in the environment (Tamerius et al., 2011). Another plausible driver of RSV seasonality is malnutrition. In many tropical settings the rainy season is a time of poor nutrition and reduced child growth (Vaitla et al., 2009; Ulijaszek and Strickland, 1993). Poor nutrition in children leads to reduced host immunity and consequently an increased incidence and severity of infection (Caulfield et al., 2004; Shell-Duncan and Wood, 1997; Zaman et al., 1996). This association been demonstrated for RSV infection (Okiro et al., 2008; Paynter et al., 2014a).

Identifying the environmental exposures driving infectious disease seasonality is difficult. Simple correlation of the seasonal patterns of exposure and infection is vulnerable to confounding if the number of infections follows a regular seasonal pattern (which is often the case) because many other environmental exposures will also vary seasonally. For this reason many studies examine associations at the day-to-day timescale, after removing the seasonal variation from incidence data. However, analysis at the seasonal time scale is vital because some environmental drivers act over long time scales. For example, day-to-day variations in nutrition would not be expected to lead to day-to-day variations in host susceptibility. How then do we examine seasonal scale associations between environmental exposures and RSV incidence while reducing the risk of confounding? One method is to focus on settings where seasonal patterns are irregular. Another is to focus on settings where one or more potential drivers are absent. Both approaches will limit the amount of confounding: the first because it is unlikely all risk factors will share the same irregular seasonal pattern, the second because the number of other risk factors (and hence potential confounders) is directly limited. We examine two such examples here.

The first example is from the Gambia. It has been noted previously that RSV epidemics have an irregular seasonal pattern in the Gambia, and so do not always occur during the regular rainy season (van der Sande et al., 2004). An alternative explanation of the observed seasonality of RSV is the seasonal variation in child nutrition and growth. Seasonal malnutrition during the rainy season is a major ecological pressure in the Gambia (Rayco-Solon et al., 2005; Ulijaszek and Strickland, 1993), exacerbated further by the increased incidence of diarrheal illness during the rainy season (Brewster and Greenwood, 1992; Ulijaszek and Strickland, 1993). We examine this hypothesis below, comparing the seasonal pattern of child nutritional status with RSV incidence.

The second example is from Florida. Despite being separated by only 520 km, Miami in Southeast Florida and Jacksonville in North Florida have differing patterns of RSV seasonality: The RSV season in Miami occurs two to three months earlier than in Jacksonville. In a high income setting such as the USA, seasonal variations in nutrition would seem to be an unlikely driver of the different seasonality in these nearby cities. In addition, the population structure of the two areas appears similar: In 2012 the percentage of the population aged less than five years was 6.3% in North Florida and 6.0% in Southeast Florida (Florida Department of Health, 2013a). One possible explanation for the differing seasonality in these two areas is climate: The climate in Southeast Florida is classified as tropical, and it is warmer and more humid than in North Florida, which is classified as temperate (Peel et al., 2007). We assessed this hypothesis by comparing the seasonal patterns of rainfall and temperature to RSV incidence in both North Florida and Southeast Florida.

2. Methods

All data used in our analyses have either been published previously, or are freely available online. Monthly numbers of RSV hospital admissions in children aged less than two years from in and around Banjul, Serrekunda and Yundum, as well as monthly rainfall data for Yundum, were taken from data published in the aforementioned Gambian study (van der Sande et al., 2004). RSV was diagnosed by antigen detection (immunofluorescence testing of nasopharyngeal aspirates taken from all children admitted with respiratory infection at the two local referral hospitals). The data covers October 1993 to October 2002. We compared the Gambian RSV data to growth data collected as part of The Gambia Nutrition Surveillance Programme (The Gambia Nutrition Surveilleance Program, 2010). In this programme, twice yearly (dry season and rainy season) surveys were performed collecting weight-for-height data from a large sample of Gambian children aged five years or less. Low weight-for-height (wasting) is indicative of acute malnutrition (World Health Organization, 2009). For our study we have defined the community level nutritional status of children at each survey as the proportion of children with weight-for-height greater than 90% of the reference median (Nabarro and McNab, 1980). We used data from the Western Region of the Gambia, which includes the area where the RSV data was collected. Nutritional data were missing for the dry season in 1995.

RSV surveillance data for Florida are available from the Florida Department of Health website (Florida Department of Health, 2013b). Sentinel hospitals throughout Florida report the total number of RSV tests performed and the total number of positive RSV tests. For our study we have defined RSV incidence as the total number of positive RSV tests per month. Meteorological data for Florida are available from the National Climatic Data Centre website (National Climatic Data Centre, 2013). We compared the monthly RSV surveillance data from Southeast Florida and from North Florida to monthly meteorological data from Miami and Jacksonville respectively.

For the analysis of the Florida data, the regular seasonal patterns permitted the use of cross-correlation over the course of the three year time series. This enabled us to compare monthly RSV incidence with meteorological data in previous months. Because of the irregular RSV peaks in the Gambian data, similar cross-correlation is not appropriate (cross-correlation gives average associations over the course of the time series, which would defeat the purpose of choosing a study setting with irregular RSV seasonality). Instead we have compared the rainfall and nutrition data to RSV incidence using simple correlation with no lag, and plotted the data to demonstrate the relative consistency of these associations over the time series.

3. Results

3.1. The Gambia

Fig. 1A shows data taken from the aforementioned Gambian study (van der Sande et al., 2004), clearly demonstrating that in the years 1997, 1999, and 2001, the yearly RSV epidemics were "late", occurring several months after the rainy season. In Fig. 1B we have superimposed the child growth data over the RSV incidence data. In the first part of the time series (1993 to 1996) the regular hungry season is evident, with poorer nutrition during the rainy season. The RSV epidemics are correspondingly regular over this period, with peak RSV activity during the rainy/hungry season. In 1997 the rainy season was not associated with the characteristic drop in nutritional status, and the RSV epidemic was notably smaller, as well as approximately three months "late". For the remainder of the time series the RSV epidemics are irregular, but appear to occur consistently at low points of nutritional status. While both nutrition and rainfall are significantly correlated with RSV incidence, nutrition is more strongly correlated (and as can be seen from Fig. 1, more consistently correlated). The correlation coefficient for nutrition and RSV is −0.73 (95% CI −0.90 to −0.38) while for rainfall and RSV it is 0.37 (95% CI 0.20 to 0.52).

3.2. Florida

Fig. 2 shows monthly RSV incidence compared to the monthly mean minimum temperature and the number of days per month with greater than 0.1 in. of rainfall. For simplicity we have not shown any humidity