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Seasonality of respiratory syncytial virus - lower respiratory tract infection (RSV-LRTI) in children in developing countries

Abstract

Respiratory Syncytial Virus (RSV), an enveloped RNA virus with a non-segmented single-stranded negative-sense genome, is the primary cause of hospitalization in the first year of life for children in most parts of the world. The global estimate in 2005 indicated that at least 33.8 million episodes of RSV associated acute lower respiratory infection (ALRI) occurred worldwide in children younger than 5 years and most of these deaths occurred in developing countries. This study aimed to systematically aggregate and analyze published epidemiological data on the seasonality of RSV lower respiratory tract infections in young children in developing countries. Articles in English published between 2002 and 2014 were identified through literature searches in PubMed, Web of knowledge, and . The season in which RSV epidemics occur typically depends on geographical location and altitude. It is likely that several factors interact in complex ways in the development of epidemics under favorable climatic conditions.

Keywords: respiratory syncytial virus, rsv; seasonality; lower respiratory tract infection; children; developing countries

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Introduction

Lower respiratory tract infection (LRTI) is the leading global cause of death in children between 1 month and 5 years of age.[1-4] Clinical characteristics of RSV infection include upper respiratory infection with rhinorrhea and nasal congestion lasting between 7 and 12 days. Re-infection rates vary between 6% and 83% each year, showing that initial infection does not confer immunity to succeeding infection.[5] By the age of 2 years, nearly all children have had RSV infection.[6] More serious disease involving the lower respiratory tract may develop in older children especially in immunocompromised and cardiopulmonary disease patients.[7,8] RSV season varies over time and from location to location.[9,10] The start and end of RSV season can vary year to year, state to state, and can even vary within communities in the same region.[9,11]

In countries with temperate climates, RSV causes epidemics of LRTI among infants and young children during late fall, winter, and early spring. In temperate climate regions, the RSV epidemic pattern depends on the temperature rather than the rainfall pattern. Most communities with temperate climates have a well-defined season of 3 to 5 months usually starting in the Northern hemisphere in October or November and continuing until February or March, followed by a peak in activity in the Southern hemisphere. In the southern hemisphere, wintertime epidemics occur from May to September. In addition, RSV studies conducted in temperate climates have identified a biannual pattern in the peak of RSV epidemics and RSV hospitalization rates, whereby the severity of RSV seasons alternates between milder and more severe. However, this is not predictable, and the differences may be more related to climatic changes.[12]

This study aimed to systematically aggregate and analyze published epidemiological data on the seasonality of RSV lower respiratory tract infection in young children in developing countries (Table 1).

Materials and methods

Potentially relevant published articles were identified through literature searches of the following bibliographic databases: PubMed, Web of knowledge, and Embase. To access publications from developing countries that might not be included in those databases, searches in SciELO, Indian MEDLARS, Bioline International, and African Journals online were also performed. The following combination of MesH terms (Medical Subject Heading terms) and individual search terms were used: (Respiratory Syncytial Viruses OR pneumonia OR bronchiolitis OR respiratory tract infections) AND (developing country OR each individual country of the developing countries) for the epidemiological review, and (Respiratory Syncytial Viruses AND vaccine) for the review of vaccine development updates. The searches were restricted to studies of human subjects that were published in English between 2002 and 2014. Manual searches of reference from potentially relevant articles were also performed to identify additional studies that may have been missed using the computer-assisted strategy. For the purpose of this review, the developing countries were defined as the ones designated as such by either World Bank (low, lower middle and upper middle-income countries) or World Health Organization. Countries with a contradiction of development status classification between World Bank and WHO were included within the developing countries group for this review.

Results and discussion

In tropical or semitropical climates, RSV outbreaks are frequently associated with the rainy rather than the colder season. The variation is less apparent in the tropics, where there is small fluctuation in ambient temperature. RSV epidemics appear regularly but with different patterns of seasonality. In northern tropical areas, the seasonality seems to be associated with a decrease in temperature and an increase in rainfall. In the equatorial regions, RSV appears to be present most of the year. There are definitely 7 to 8 months of the year when the prevalence is higher than in the other 4 or 5 months, with some increase during the dry months. Tropical areas south of equator have a seasonality that is associated with decrease in both temperature and rainfall. Geographic and climatic factors are clearly associated with epidemics, but it is uncertain whether this is related to spread

of the virus, behavioral factors, or cyclic changes in a population's immunologic susceptibility.[13,14]

The concept of RSV epidemic seasonality across continents and within geographic areas has been addressed in some of the reviewed publications. Here we present a summary of the publications from Africa, Latin America, Eastern Mediterranean, Europe, Southeast Asia and Western Pacific.

Africa

Reviewed articles were from Southern Africa, West Africa, and East Africa. No information on seasonality could be obtained from or Central and North Africa. The association of RSV epidemic periods with the wet seasons in tropical African countries is similar to observations of other studies from tropical countries with seasonal rainfall. The typical RSV season corresponded to the cold season in South Africa, where a temperate climate is observed. The discrepancy found within the countries might be due to interannual variation on viral seasonality.

The epidemic peak generally starts early in east African countries (Kenya, Mozambique) and South Africa then progresses to the West African countries (Senegal, Gambia, Ghana, Nigeria). The overall picture of RSV seasonality is in line with a previous publication describing that epidemics start at the very southern coast of Africa during the early period of the year and then move northward during the next 6 months.[13] The isolation of RSV throughout the year in some African countries may be explained by the tropical climate and the concurrent HIV epidemic in the population which results in prolonged carriage of RSV and less evident seasonality.

Latin America

The seasonality studies in Latin America are from 4 countries -Mexico, Brazil, Argentina, and Chile. Mexico experiences the earliest RSV season, followed by Argentina and Chile. The seasonality of the RSV epidemics agrees with data from a previous study which found that epidemics occurred from north to south in South America.[13] Studies from Brazil have shown a diversified seasonal pattern for RSV, probably related to the wide diversity of climate characteristics in the country. While in the north,[15-31] rainfall is the main climatic determinant, temperature variations play a more significant role in the south. RSV infections peaked in the coldest months in southern Brazil,[32] the only region with temperate climate, similar to that observed in Argentina and Chile. In southeast region, the peak of RSV outbreaks have not been associated with rainy seasons nor the coldest months and the epidemics appeared to spread throughout many months[33-40] with one study detecting RSV cases throughout the year[41] (Table 2).

Eastern Mediterranean

In desert climates, RSV infection has been associated with the cold season, a finding consistent with the pattern found in this review.[14] The study from United Arab Emirates provided inconclusive data defining RSV seasonality as it was conducted for only 3 months (September to November).[54] Seven out of eleven studies from the Eastern Mediterranean were spanned only for short periods less than 12 months, and probably were insufficient to obtain information on seasonality[42-57] (Table 3).

Europe

The quality and quantity of RSV seasonality information of developing European countries within the past 10 years was poor, and each available study covered only short periods (5-8 months).[58-60] Additionally, a study from Russia reported an unexpected factor of climate abnormality as a reminder that a single season may not be representative of the RSV season from year to year.[58] Broader and longer studies should be considered in the developing European region (Table 4).

Southeast Asia and western pacific

In the Southeast Asia region, epidemics occur in the equatorial region first (Indonesia), then appear in the countries above the equator during the following months. (Thailand, Vietnam, Malaysia), similar to the observation in an earlier study.[13]

In the Indian subcontinent, RSV seasons started from Pune in west India[61] and Dhaka in Bangladesh,[62] followed by Bhaktapur in Nepal,[63,64] New Delhi[65,66] and Ballabgarh in north India.[67] The epidemics followed a south to north progression as previously described, except one study from Kolkata, India[68] where the RSV season was typically earlier during the rainy season.[13,14] Nevertheless, this study has shown contradictory results. There is a potential for substantial regional and geographic differences of RSV seasonality in China but only 3 studies were published in English and retrieved from the literature search.[69-72] Huge population, results discrepancy and evidence of climate change in China warrant further studies (Table 5).

Table 1 Seasonality of RSV respiratory illnesses in Africa

Country / Location	Study Period	Peaked Season	Peaked Months JAN FEB MAR APR MAY JUN JUL AUG SEP OCT NOV DEC
Mozambique, Manhica [15]	Feb 99 - Jan 00	Rainy	
Mozambique, Manhica [16]	Oct 98 - May 00	Rainy	
Mozambique, Manhica [17]	Sep 06 -Sep 07	Winter	
Kenya, Kilifi [18]	Jan 02 -Jan 03	Rainy	
Kenya, Kilifi [19]	Jan 02 -Dec 07	Rainy	
Kenya, Kilifi [20]	Jan 07 - Dec 07	Rainy	
South Africa, Durban [21]*	Jun 99 - May 00	Rainy	
South Africa, Johannes berg [22]	Mar 98 - Dec 04	Autumn - winter	
South Africa, Johannesburg [15]*	Apr 00 -Mar 01	Winter	
Nigeria, Ibadan [15]*	Jun 99 - May 01	Dry	
Nigeria, Ibadan [23]	n/a	Rainy	
Ghana, Kumasi [24]	Jan 08 - Dec 08	Rainy	
Senegal, Sine Saloum [25]	Jul 07 -Dec 07	Rainy	
Gambia, Banjul [26]*	Oct 93 - Oct 02	Rainy	
Gambia, Fajara, Sibanor [27]	Oct 93 - Dec 97	Rainy	

RSV peaked months shaded *=detected throughout year.

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Table 2 Seasonality of RSV respiratory illnesses in Latin America

Country / Location	Study Period	Peaked Season	Peaked Months
			JAN FEB MAR APR MAY JUN JUL AUG SEP OCT NOV DEC
Mexico, San Luis Potosi [42]	May 03 - Apr 05	Winter	
Mexico, Mexico city [43]	Jan 97 – Feb 98	Spring	
Mexico, San Luis Potosi [44]	Apr 09 – Mar 10	Winter	
Brazil, Fortaleza (NE) [30]	Jan 01 – Jul 04	Rainy	
Brazil, Recife (NE) [29]	Jun 94 – Jun 95	Winter	
Brazil, Salvador (NE) [28]	Jan 98 – Dec 98	Rainy	
Brazil, Salvador (NE) [31]	Sep 03 – May 05	Rainy	
Brazil, Uberlandia (SE) [36]	2001 – 2004	Autumn	
Brazil, Uberlandia (SE) [34]	Apr 00 – Jun 03	Autumn	
Brazil, Vitoria (SE) [41]**	Jul 97 – Jun 98	Summer to autumn	
Brazil, Sao Paulo (SE) [39]	May 04 – Sep 05	Autumn to winter	
Brazil, Sao Paulo (SE) [40]	May 04 – Sep 05	Autumn to winter	
Brazil, Sao Paulo (SE) [33]	Sep 00 – Nov 01	Autumn to winter	
Brazil, Sao Paulo (SE) [35]	Apr 04 – Sep 04	Autumn	
Brazil, Sao Paulo (SE) [37]	Jan 03 – Dec 03	Autumn to winter	
Brazil, Sao Paulo (SE) [38]	Feb 05 – Sep 06	Autumn to winter	
Brazil, Rio Grande do Sul (S) [32]	May 90 – Sep 90	Winter	
Brazil, Rio Grande do Sul (S) [32]	May 91 – Dec 92	Winter	
Argentina, Buenos Aires [45]	Jan 98 – Dec 02	Winter	
Chile, Santiago [46]	Jan 89 – Dec 00	Winter	

RSV peaked months shaded **=detected throughout year except August and December, N/A = not available.

NE =Northeast Brazil, SE=Southeast Brazil, S=Southern Brazil.

Table 3 Seasonality of RSV respiratory illnesses in Eastern Mediterranean

Country / Location	Study Period	Peaked Season	Peaked Months
			JAN FEB MAR APR MAY JUN JUL AUG SEP OCT NOV DEC
Iran, Tehran [47]	Nov 97 – Mar 98	Winter	
Iran, Rasht [48]	Nov 03 – Mar 04	Winter	
Iran, Tehran [49]	Mar 08 – May 09	Winter	
Jordan, Amman [50]	Sep 02 – Mar 04	Winter	
Jordan, Amman [51]	Dec 03 – May 04	Winter	
Jordan, Amman [52]	Jan 07 – Mar 07	Winter	
Kuwait, Kuwait city [53]	n/a	Winter	
UA Emirates, Abu Dhabi [54]	Sep 01 – Nov 01	Winter	
Egypt, Cairo [55]	Dec 06 – Nov 07	Winter	
Pakistan, Islamabad [56]	Oct 99 – Apr 00	Winter	
Yemen, Sana'a [57]	Oct 02 – May 03	Winter	

RSV peaked months shaded.

Table 4 Seasonality of RSV respiratory illnesses in Europe

Country/Location	Study Period	Peaked Season	Peaked Months
			JAN FEB MAR APR MAY JUN JUL AUG SEP OCT NOV DEC
Serbia, Belgrade [59]	Nov 08 - Mar 09	Winter	
Turkey, Istanbul [60]	Oct 06 - Mar 07	Winter	
Russia, St. Petersburg &Tomsk [58]	Sep 08 -Apr 09	Spring	

Table 5 Seasonality of RSV respiratory illnesses in Asia and Western Pacific

Country/Location	Study Period	Peaked Season	Peaked Months
			JAN FEB MAR APR MAY JUN JUL AUG SEP OCT NOV DEC
Indonesia, Cikutra & Ujung berung [68]	Feb 99- Jan 01	Rainy	
Indonesia, Lombok island [69]	Jan 00-Dec 02	Rainy	
Indonesia, Cikutra & Ujung berung [70]	Feb 99-May 01	Rainy	
Indonesia, Lombok island [71]***	Jan 00-Dec 01	Rainy	
Indonesia, Lombok island [72]	Jan 99-Dec 01	Rainy	
Malaysia, Kuala Lumpur [73]*	1982- 2008	Rainy	
Malaysia, Kuala Lumpur [74]	Jan 82- Dec 97	Rainy	

Citation: Sricharoenchai S, Palla E, Sanicas M. Seasonality of respiratory syncytial virus - lower respiratory tract infection (RSV-LRTI) in children in developing countries. *J Hum Virol Retrovirol.* 2016;3(1):1–6. DOI: 10.15406/jhvrv.2016.03.00076

Table Continued...

Country/Location	Study Period	Peaked Season	Peaked Months
			JAN FEB MAR APR MAY JUN JUL AUG SEP OCT NOV DEC
Malaysia, Kelantan [75]	Jan 01- Dec 01	Rainy	
Thailand, Khon Kaen [76]	Apr 02-Aug 04	Rainy to winter	
Thailand, Bangkok [77]	Dec 07- Aug 09	Rainy to winter	
Thailand, Nakhon Sawan [78]	Nov 98-Feb 01	Rainy	
Thailand, Nakhon Sawan [79]	Nov 98- Feb 01	Rainy	
Thailand, Sakaeo & Nakorn Panom [80]	Sep 03- Dec 07	Rainy	
Thailand, Sakaeo & Nakorn Panom [81]	Sep 03- Dec 05	Rainy	
Vietnam, Nha Trang [82]	Feb 07-Mar 08	Rainy	
Vietnam, Ho Chi Minh [83]	Nov 04 -Jan 08	Rainy	
India, Pune [61]	Feb 02- Dec 04	Rainy	
India, Kolkota [68]	Jan 07- Dec 08	Winter	
Bangladesh, Dhaka [62]	1993 – 1996	Monsoon	
Nepal, Kathmandu [63]	Jul 04- Jun 07	Monsoon & winter	
Nepal, Kathmandu [64]	Jan 06- Jun 08	Monsoon & winter	
India, New Delhi [66]	Jan 07 -Dec 07	Winter	
India, New Delhi [65]	Apr 05- Mar 07	Autumn	
India, Ballabgarh [67]****	Oct 01-Mar 05	Autumn to winter	
China, Lanzhou [84]*****	Dec 06- Mar 09	Winter to spring	
China, Shanghai [85]	Oct 06- Sep 08	Autumn to winter	
China, Zhejiang [86]*	Jan 01- Dec 06	Winter to spring	

*= detected throughout the year.

*** = detected throughout the year except September to November.

**** = detected throughout the year except July and August (rainy season).

*****= detected throughout the year except July, August and September.

Limitations of the current literature review

Despite various literature databases utilized to make this review as exhaustive as possible, some limitations exist.[73] Only English literature was searched. This likely biased the findings by excluding some studies from certain regions such as China, and some countries in Latin America, Russia, and the Middle East where there may be substantial information in local language publications.[74-76]

Conclusion

The season in which RSV epidemics occur typically depends on geographical location and altitude. It is likely that several factors interact in complex ways in the development of epidemics under favorable climatic conditions [77]. Despite the increasing number of epidemiological studies of RSV-LRTI published over the past decade in developing countries, there are still clearly many areas that merit further study.[78-80] There is still a need to establish further RSV surveillance studies to improve the incidence estimates and to explore the extent to which national and regional variation in RSV infection rates exist in countries where there is a high burden and high mortality attributable to LRTI but lack of understanding of local RSV epidemiology. Future epidemiological studies should be conducted over adequate time periods to offset bias from temporal variation and to assess the long term variability of RSV seasonality.[81-85] Baseline data on incidence and seasonality of each geographic region can be useful in planning RSV vaccine trials in various geographies.[86]

Author contribution

SS, EP and MS contributed to the design and interpretation of data for this manuscript. SS, MS and DD were responsible for drafting the work and revising it critically for intellectual content. All authors agree to be fully accountable for ensuring the integrity and accuracy of the work and read and approved the final manuscript.

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Conflicts of interest

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