American Journal of BioScience
2021; 9(6): 185-191
http://www.sciencepublishinggroup.com/j/ajbio
doi: 10.11648/j.ajbio.20210906.13
ISSN: 2330-0159 (Print); ISSN: 2330-0167 (Online)

Surveillance of Respiratory Syncytial Virus in Children Aged 0-5 years in Côte d'Ivoire

Venance Kouakou[1, 2, *], Hervé Kadjo[1], N'nan Alla Oulo[2], Fidèle Diobo N'guessan[1, 3], Adèle N'Douba[4]

[1]Respiratory Virus Unit, Institute Pasteur of Côte d'Ivoire, Abidjan, Côte d'Ivoire

[2]Genetics Laboratory, Felix Houphouët Boigny University, Abidjan, Côte d'Ivoire

[3]Parasitology Laboratory, Felix Houphouët Boigny University, Abidjan, Côte d'Ivoire

[4]Microbiology Teaching Unit, Felix Houphouët Boigny University, Abidjan Côte d'Ivoire

Email address:

lucvenance0@yahoo.fr (V. Kouakou)

[*]Corresponding author

To cite this article:

Venance Kouakou, Hervé Kadjo, N'nan Alla Oulo, Fidèle Diobo N'guessan, Adèle N'Douba. Surveillance of Respiratory Syncytial Virus in Children Aged 0-5 years in Côte d'Ivoire. *American Journal of BioScience*. Vol. 9, No. 6, 2021, pp. 185-191.
doi: 10.11648/j.ajbio.20210906.13

Received: October 11, 2021; **Accepted**: November 13, 2021; **Published**: November 19, 2021

Abstract: Acute Respiratory Infections (ARI) are, after malaria, the second most common cause of consultation of children in health facilities in Côte d'Ivoire. Viral etiology points to Respiratory Syncytial Virus (RSV) as the primary cause of these acute respiratory infections. In order to better assist health workers in diagnosing the virus, a study on the epidemiology, seasonality and clinical signs associated with RSV acute respiratory infections was conducted over four consecutive years. During these years, nasopharyngeal samples were collected from 5648 children aged 0-5 years, in different geographical areas of the country, following a survey form for analysis by real-time PCR, to detect the virus and describe its epidemiological characteristics. Our results revealed 564 (9.98%) RSV positive children. A number of 181 (32.09%) were positive in inpatients, and 383 (67.91%) in outpatients. The 0-12 month age group was the most affected with 51.95% of positive cases. Cumulative monthly RSV activity for the 4 years of the study was relatively lower during the months of January to March and higher during the months of May to September. This distribution of RSV was superimposed on rainfall during these study years. Our work has also linked RSV positivity to the presence of clinical signs, including fever, cough, diarrhoea and vomiting. These results give scientific tools to health personnel to better orient their diagnosis and also a better rational use in the prescription of medication, notably the stopping of unjustified antibiotic therapy.

Keywords: Respiratory Syncytial Virus, Surveillance, Children, Seasonality

1. Introduction

Acute respiratory infections (ARIs) are infections that affect the respiratory system, nose, throat, larynx, trachea, bronchioles and lungs [1]. Depending on the level of damage to the respiratory tree, a distinction is made between high and low ARI [2]. Bronchiolitis, pneumonia and bronchitis are the conditions that result from these lower respiratory tract infections in children. Several studies [3, 4] have shown that respiratory syncytial virus (RSV) is the most important viral pathogen involved in acute respiratory infections (ARI) in children under 5 years of age. Its burden is estimated at 33.1 millions episodes, with nearly 3.2 millions hospitalizations and 59.600 deaths worldwide in 2010 [5]. Of the 154,000 acute respiratory infections in Africa, 14,920 were reported in West Africa for RSV respiratory infection by Njouom and *al* [6]. This burden would be underestimated, as health systems in low- and middle-income African countries are very fragile [5]. Therefore, these figures may not reflect the true burden of the virus responsible for these infections on the population, especially the child population.

In Côte d'Ivoire, acute respiratory infections are the second most frequent cause of consultation with health specialists [7]. Kadjo and *al* reported in their work that RSV is responsible for respiratory infections in children under five years of age in Côte d'Ivoire [8]. Azagoh-Kouadio and *al* showed a persistence of

respiratory infections in children aged 0-5 years [9]. However, very little information is available on the prevalence, seasonality of the virus, and clinical signs associated with RSV in the 0-5 years old population in Côte d'Ivoire. Given the regular admission of antibiotics due to probabilistic clinical diagnosis and the impact of the respiratory virus on the child population, it is important to put in place effective preventive and therapeutic strategies for better clinical management and rational use of antibiotics. The objective of this work is to provide general knowledge on the epidemiology of the virus, its seasonality and the signs associated with RSV in children aged 0 to 5 years in Côte d'Ivoire, over the four years of study from January 2016 to December 2019.

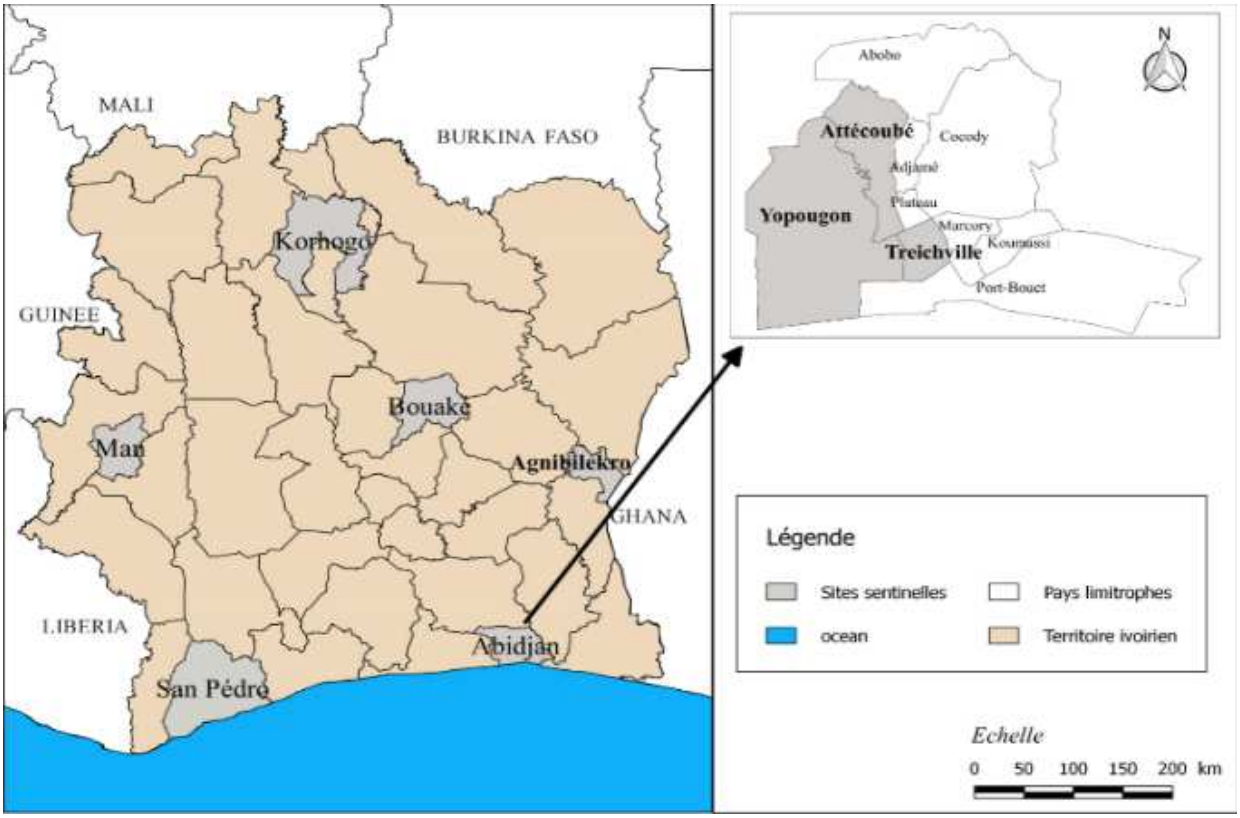


Figure 1. *Map of study sites.*

2. Materials and Methods

2.1. Study Design

This study is a cross-sectional and descriptive study on nasopharyngeal samples, collected in different sites of the national influenza surveillance network in Côte d'Ivoire (Figure 1). Theses site are 3 in Abidjan (Attécoubé, Yopougon, Treichville), 5 in the interior of the country (Bouaké, Korhogo, San pédro, Man, Agnibilekro) and are supplemented with a prison environment. These sites consist of 2 University Hospitals (CHU), 3 Regional Hospitals (CHR), 2 General Hospitals (HG) and a Community Urban Health Unit (FSU COM). The selection of these sites is based on the following criteria: the daily flow of patients in consultation, the existence of a department of general medicine and a department of paediatrics, the willingness and availability of doctors to participate voluntarily without financial motivation and the availability of a refrigerator (+4C°) for the storage of samples.

2.2. Suspect Case Definition

Biological sampling of a patient was carried out if they met the definition of a suspected case. All patients seen in consultation or hospitalised for a respiratory infection aged between 1 month and 5 years, and a temperature ≥ 37°C with cough or sore throat were included in this study.

2.3. Epidemiological Information

Demographic data (age, sex, health region) and clinical data before and at the time of sample collection were collected from the forms and recorded in an Access database once in the laboratory. The database was exported to an Excel spreadsheet for statistical analysis. For each patient included in the study, a form was rigorously filled in to collect socio-demographic data (region of origin, health district, sentinel site, age, sex), followed by clinical symptoms observed during consultation or hospitalisation. Four of these symptoms such as cough, fever, diarrhoea and vomiting, were mainly sought during our study. A clinical history was taken by the sentinel site physician to determine the clinical factors associated with RSV ARI.

2.4. Sample Collection and Transport

A nasopharyngeal swab was taken from each child

meeting our case definition and immediately stored in a sterile cryovial containing viral transport medium (VTM). The samples were transported by land from the sentinel sites to the National Influenza Centre (NIC) located at the Pasteur Institute of Côte d'Ivoire. A delay of 3 days between the date of collection and the date of receipt at the laboratory is taken into account as an indicator of sample viability. Samples were collected weekly.

2.5. Extraction and Amplification of Biological Material

RNA from 5648 nasopharyngeal samples was collected using the Qiagen RNA extraction kit (QIAamp® Viral RNA, Germany), as recommended by the manufacturer. RSV was tested in the RNA extracts by RT-qPCR using the CDC Respiratory Syncytial Virus Real-Time RT-PCR diagnostic kit (CDC, Atlanta, USA), targeting the nucleoprotein gene. The master mix was performed on a reaction mixture with a final volume of 20µl. The components were: 12.5µl of AgPath-IDTM One-Step RT-PCR 2X buffer, 1µl of AgPath-IDTM One-Step RT-PCR enzyme, 0.5µl of each primer and probe at 200nM each, and 5µl of molecular water. For each sample, 5µl of RNA was added. The primers used are as follows:

Forward 5'-GGC AAA TAT GGA AAC ATA CGT GAA-3',

Reverse 5'- TCT TTT TCT AGG ACA TTG TAY TGA ACA G-3',

Probe 6FAM- CTG TGT ATG TGG AGC CTT CGT GAA GCT-BHQ.

The results were visualised using a thermal cycler (Applied Biosystems 7500) under the following conditions: 10 min at 50°C and 10 min at 95°C, followed by 45 cycles of 15 s at 95°C and 1 min at 55°C.

2.6. RSV Epidemiology

Demographic data (age, sex, health region) and clinical data before and at the time of sample collection were collected from the forms and recorded in an Access database once in the laboratory. The database was exported to an Excel spreadsheet for statistical analysis.

2.7. RSV Seasonality

The distribution of molecular data obtained by RT-qPCR by month and year of the study period was used for correlation with climatological factors (cumulative precipitation (mm), mean relative humidity (%) and mean ambient temperature (°C)). The Exploitation Society of Airline and Metrology (SODEXAM) provided the climate data for each of the study sites.

2.8. Statistical Analyses

The relationship between explanatory (climatic, epidemiological and clinical factors) and explained (monthly distribution of RSV) factors was performed using R software version x64.4.0.2. Statistical significance was defined as $p \leq 0.05$.

2.9. Ethical Consideration

Informed consent was obtained from parents before any nasopharyngeal swab aspiration. Data included in the study were anonymised to avoid identification of patients and prescribers. Patients' place of residence, occupation and telephone numbers were removed from the database. In addition, access to the database was restricted to unauthorised persons. We have obtained permission from the National Influenza Centre of the Pasteur Institut of Côte d'Ivoire to use these data strictly for the purposes of this publication.

3. Results

3.1. Epidemic Characteristics

From 2016 to 2019, a total of 5648 respiratory specimens were collected from the different sentinel health centres in the country. The sites in the interior of the country collected 55.01% (3107/5648) of all specimens, with a large share for the site of Man with 1427/5468 specimens, followed by the site of Attecoubé with 1305/5468. All the children included had presented symptoms of acute respiratory infections according to WHO criteria. Men were the most representative of the study population with 53% compared to 47% of women, with. a sex ratio of 1.17. Patients with severe acute respiratory infection (hospitalized) represented 31.94% (1804/5648) of the included population. A number 3325 children (58%) were aged 0-12 months, 1137 (20.13%) were aged 13-24 months, 696 (12.32%) were aged 25-36 months and 490 (8.68%) were aged over 36 months. The distribution of acute respiratory infection cases was significant (*p=0.003*) to the age distribution of the included population (Table 1). The clinical history collected from the study population was dominated by malnutrition (47.21%) followed by pneumonia (30.90%). Asthma, immune deficiency, heart disease and obesity accounted for 17.16%, 2.14%, 1.71%, 0.88% of the clinical history respectively (Table 1). Cough and fever were at the forefront of the clinical picture with 97.45% and 96.33% of patients respectively. Vomiting was less frequent with 21.88%, as well as diarrhoea (12.85%) in patients (Figure 2).

Table 1. *Characteristics of the study population.*

Variables	Category	Number Rsv (5648)	Rsv Positive (564)	Rsv Negative (5084)	*P Value*
Gender	Male	3036 (53)	307 (54,43)	2 729 (53,67)	*0,94*
	Female	2612 (47)	257 (45,57)	2 355 (46,33)	
Age (month)	1-12	3325 (58)	293 (51,95)	2958 (58,18)	*0,003*
	13-24	1137 (20)	138 (24,46)	1024 (20,14)	
	24-36	696 (12,3)	99 (17,55)	646 (12,70)	
	≥ 36 mois	490 (8,6)	34 (6,04)	456 (8,98)	

Variables	Category	Number Rsv (5648)	Rsv Positive (564)	Rsv Negative (5084)	*P Value*
Status	Hospitalized	1804 (31)	181 (32,09)	1623 (31,92)	*0,99*
	Ambulatory	3 844 (68)	383 (67,91)	3461 (68,08)	
Clinical status of the patient	Asthma	40 (17,16)	3 (0,53)	37 (16,97)	*0,13*
	Heart disease	4 (1,71)	1 (0,17)	3 (1,37)	
	Immune deficiency	5 (2,14)	2 (0,35)	3 (1,37)	
	Malnutrition	110 (47,2)	3 (0,53)	107 (49,08)	
	Respiratory disease	72 (30,90)	6 (1,06)	66 (30,27)	
	Obesity	2 (0,88)	0	2 (0,94)	

() percentage value.

Table 2. *Distribution of cases by clinical symptoms.*

Clinical symptoms	RSV positive (564)	RSV negative (5084)	*P*
Cough	546 (96,80 %)	4958 (97,52 %)	*0,0009*
Vomiting	92 (16,31 %)	1144 (22,50 %)	
Diarrhoea	48 (8,5 %)	678 (13,33 %)	
Fever	549 (97,34 %)	4892 (96,22 %)	

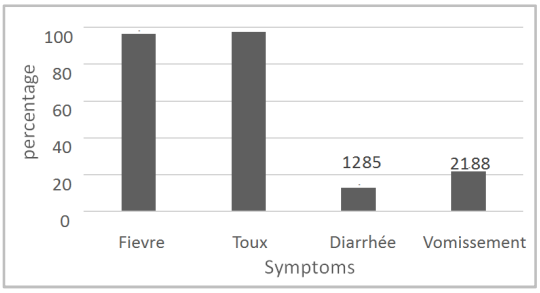


Figure 2. *Frequency of clinical signs in the study population.*

Table 2 shows the distribution of the biological status of the study population after virus testing for the different symptoms considered on admission. RSV positivity was significantly related to the presence of clinical symptoms (*0,0009)*.

3.2. RSV Seasonality

The cumulative monthly viral activity of the four years of Respiratory Syncytial Virus was highest in the months of May to September and relatively lower in the months of January to March (Figure 3). However, for the year 2017, the peak of infections was observed in the months of August and September. The years 2017 and 2019 showed a wide distribution of the virus in contrast to the years 2016 and 2018 which showed low virus infection. Regarding the influence of climatic parameters on RSV infection, it was found that the peak times of virus activity over the period 2016-2019 were comparable to an increase in rainfall at these times (Figure 4).

However, none of the other climatic factors showed the same peak times of infection. An upsurge in RSV-related illness has been observed during most rainy seasons. In 2017, the virus was detected in almost all of the Great Rainy Season (GSS) and the Little Rainy Season (LRS), as well as in the Little Rainy Season (LRS) of 2018. During 2019, positive RSV cases were observed from the GSP to the PSS. The year 2016 did not have a major distribution of positive cases by season (Figure 5).

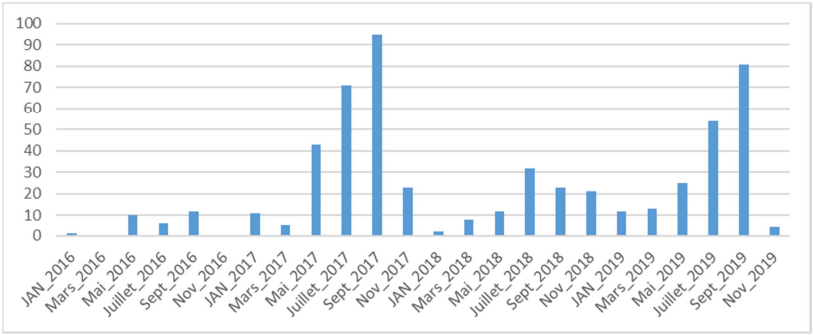
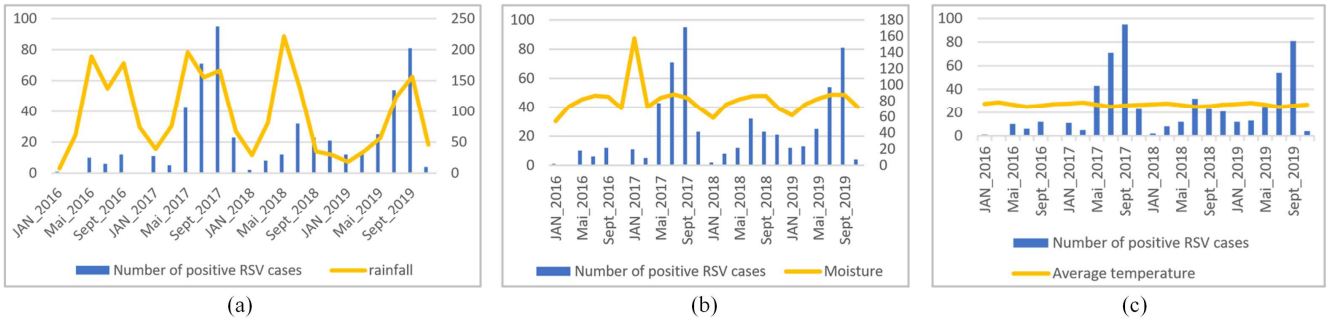
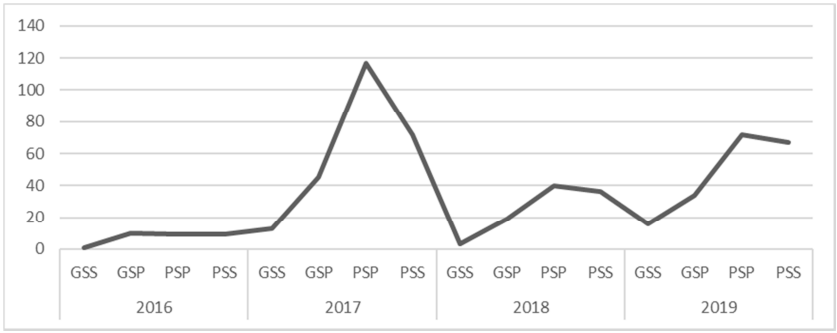


Figure 3. *Bimonthly distribution of RSV cases positifs 2016 to 2019.*



(a) (b) (c)

Figure 4. *Evolution of RSV respiratory infection in children aged 0-5 years according to climatological factors from 2016 to 2019.*



GSS: Great Dry Season; GSP: Great Rainy Season; PSP: Little Rainy Season; PSS: Little Dry Season.

Figure 5. *Seasonal evolution of Respiratory Syncytial Virus, 2016-2019.*

4. Discussion

In this study, we performed for the first time, the epidemiology of Respiratory Syncytial Virus, from nasopharyngeal aspirations of children (0 to 5 years), from January 2016 to December 2019 in Ivory Coast.

4.1. Characteristics of the Study Population

Of the 5648 samples tested, 564 or 9.98%, were positive for RSV. This proportion of positive cases varies from one country to another. Our results are lower than those reported in the literature from African countries including Senegal, Nigeria and Ghana [10, 11] with respectively 11.4%, 23% and 17.7% positive for RSV in children aged 0-5 years, using conventional PCR. The possible reasons for the different studies could be explained in the inclusion criteria for the study population, the diagnostic methods used, the climate and the duration of the study. Compared to the above mentioned studies, the low prevalence recorded in our study is explained by the study population which was the highest and the molecular diagnostic technique used. The diagnostic tools used to identify RSV respiratory viral infections have evolved. Conventional PCR has been shown to be significantly less efficient than real-time PCR (qPCR). False negatives may be associated with the inefficiency of the gel electrophoresis detection system in conventional PCR, as it can leave samples with lower levels of RSV than real-time PCR. The work of Mentel and alfound that real-time PCR was 25% more sensitive than conventional PCR for the detection of RSV [12].

The majority of RSV infections (293/564 or 51.95%) were observed in children less than 12 months of age during our work, this has been noted by previous studies [13-16]. This high rate of infection for this group of children is due to the immaturity of their immune system. The predominance of RSV infection in male children, with a rate of 54.43%, was also observed in the work of Ouédraogo and *al*, Hamzé and *al* (2010) in Burkina Faso and Liban respectively, with rates of 58.1% and 72% [17, 18]. This male predominance of RSV observed in these different studies could be due to the narrowness of the bronchi in boys, but this remains unclear [17].

The main clinical histories found in RSV-infected children in this study were pneumonia, asthma, malnutrition, immunodeficiency and heart disease. These clinical histories were not significant (p=0.13) with the distribution of infection in children. However, they are also not insignificant for the severity of RSV pathology. Welliver et al. (2003) identified pulmonary or cardiac dysplasia and immune deficiencies as classic predisposing factors for RSV infection [19]. other factors have been identified [20] including prematurity (at 33 weeks) and, to a lesser degree, genetic predisposition [21]. At inclusion, four symptoms were sought in the patients. These were fever, cough, diarrhoea and vomiting. They are not very specific to RSV infections as they are also observed in several other infectious and non-infectious diseases. The p-value (p=0.0009) between the clinical signs at inclusion and the distribution of the study population shows that RSV infection could be clinically characterised by these symptoms. Knowledge of the clinical characteristics of RSV-infected populations is important because, according to the WHO, it allows standardized case definitions of acute respiratory infections in humans to be obtained that are applicable to all countries. It also allows for comparison of results between different countries and regions to provide characteristics of the infection and improve control [22]. In this work, fever, which should be 100% of the patients to be in agreement with the inclusion definition, was not the case, as some patients had to be medicated for fever before their consultation by the sentinel site physicians. The cough is justified by the pathogenesis of viral respiratory infections. The viruses will cause irritation and inflammation (swelling, redness, pain, heat) of the nasal mucosa accompanied by excessive mucus production, at which point coughing becomes the body's way of avoiding mucus accumulation in the lungs. Diarrhoea and vomiting are digestive signs in response to the viral infection. Clinical features almost similar to ours have been observed [23-25]. Almost similar proportions of fever (98%) were observed in Abidjan in 2000 [26]. Fever and cough are high because they are worrying signs for the parents, leading them to the health structures. A plausible explanation for this increase in the signs included would be the increasing environmental pollution, and the obvious parameters of climate change which does not allow the maturation of the immune system of children [27].

4.2. Seasonality of RSV

During the four years of surveillance, RSV was present during all periods of the year, from January to December, but peaked during the months of May to September. This shows that at this time of year, RSV is indeed an important causative agent of acute respiratory infections in the surveillance focal points in Côte d'Ivoire. This seasonal pattern is very consistent with that reported in Ghana [11], a country located at the same latitude, unlike in Senegal [28] and Cameroon [25]. Several authors explain that globally, RSV epidemics occur in the southern hemisphere between March and June and conversely in the northern hemisphere between September and December [29, 30].

The seasonality of RSV in Côte d'Ivoire could allow optimization of future vaccination strategies, such as timing of administration (year-round or seasonal), target population (infants or others), as the World Health Organization predicts that a vaccine against RSV will be available within 5-10 years [31]. A strong relationship between several climate variables and the RSV cycle has been shown [32].

The results of our work indicate that only rainfall was found to be superimposable with RSV distribution among the climatic factors studied. This assertion is similar to that of several tropical environments, such as Indonesia, Malaysia, the Philippines and Thailand [33-35]. Little has been published in Africa on the relationship between rainfall and RSV seasonality, however the striking similarity in the role of rainfall for influenza [36], and RSV suggests parallel transmission mechanisms for both viruses [37].

5. Conclusion

Our research work shows that respiratory syncytial virus occupies an important place in the child population and indicates the presence of the virus during the rainy seasons of each year, between May and September. Our results also identified children under 24 months of age as being more susceptible to RSV infection. In addition to cough and fever, which are important clinical signs of acute respiratory infections, diarrhoea and vomiting should be associated with diagnostic signs of respiratory syncytial virus in children. This differents parameters allow into health agents to better diagnostic adjustment. Through this scientific article, it would be important to encourage health personnel to prescribe a biological test for the early detection of RSV in children aged 0 to 5 years with acute respiratory infection, during the months of May to September in Côte d'Ivoire. Consider also the admission of a targeted therapy against RSV-related pathologies.

Acknowledgements

We extend our thanks to all participants department of epidemic viruses of Pasteur Institute côte d'ivoire. We cannot conclude without expressing our heartfelt thanks also to Influenza Division of CDC-Atlanta.

References

[1] Simoes A, F., Cherian T., Chow J., Shahid-Salles S, A., Laxminarayan R., John T. J. (2006). Acute respiratory infections in children, In: Diseases Control Priorities in developing countries, Chapter 25. Oxford University Press, New York: 1400p.

[2] Shabir A, M., Keith P, K. (2006). Acute respiratory infections, In: Disease and Mortality in Sub-Saharan Africa, Chapter 11. World Bank, 2nd edition, Washington.

[3] Hall C, B., Weinberg G, A., Iwane M, K. (2009). The burden of respiratory syncytial virus infection in young children. New England Journal Medecine, 60, 588-98.

[4] Zhou H., Thompson W, W., Viboud C, G. (2012). Hospitalizations associated with influenza and respiratory syncytial virus in the United States, 1993-2008. Clinic Infection Disease; 54, 1427-36.

[5] Njouom R., Sebastien K., Bigna J., Estelle A, W., Fredy BNS., Véronique B, P., Astrid V. (2018). Prevalence of human respiratory syncytial virus infection in people with acute respiratory tract infections in Africa: A systematic review and meta-analysis. Influenza Other Respiratory Viruses 12: 793-803.

[6] Nair H., Nokes D, J., Gessner B, D., Dherani M., Madhi A., Singleton R., O'Brien K., Roca A., Wright, P, F., Bruce N. (2010). Global burden of acute lower respiratory infections due to respiratory syncytial virus in young children: A systematic review and meta-analysis. Lancet Lond. England, 375, 1545-1555.

[7] OMS. 2010. Grippe saisonniere. Maladies transmissibles profil épidémiologique: côte d'ivoire. 83-92. 304p.

[8] Kadjo H. (2013). Sentinel surveillance for influenza and other respiratory viruses in Côte d'Ivoire, 2003-2010. Influenza and Other Respiratory Viruses 7 (3), 296-303.

[9] Azagoh-Kouadio R., Couitchéré G, L., Assé K, V., Enoh S, J., Sindé K, C., Aholi W, J, M., Oulaï S, M. (2017). Acute community-acquired pneumonia in children aged 0 to 5 years at the Treichville University Hospital in Abidjan, Côte d'Ivoire. EDUCI. Revue internationale science medicale d'abidjan -RISM 2017, 19, 4: 286-292.

[10] Fall A., Dia N., Cisse E, K., Kiori D, E., Sarr F. D., Sy S. (2016). Epidemiology and Molecular Characterization of Human Respiratory Syncytial Virus in Senegal after Four Consecutive Years of Surveillance, 2012 2015. *PLoSONE 11* (6): e0157163. Doi: 10.1371/journal.spo ne. 0157163.

[11] Obodai E., Odoom J, K., Adiku T., Goka B., Wolff T., Biere B. (2018). The significance of human respiratory syncytial virus (HRSV) in children from Ghana with acute lower respiratory tract infection: A molecular epidemiological analysis, 2006 and 2013-2014. PLoS ONE 13 (9): e0203788. https://doi.org/10.1371/journal. pone.0203788.

[12] Mentel R., Wegner U., Bruns R., Gürtler L. (2003). Real-time PCR to improve the diagnosis of respiratory syncytial virus infection. Journal Medecine Microbiology; 52 (10): 893-6.

[13] Auksornkitti V., Kamprasert N., Thongkomplew S., Suwannakarn K., Theamboonlers A., Samransamruajkij R. (2013). Molecular characterization of human respiratory syncytial virus, 2010- 2011: identification of genotype ON1 and a new subgroup B genotype in Thailand. Archive of. Virology, 159: 499-507.

[14] Baek YH, Choi EH, Song M-S, Pascua PNQ, Kwon H, Park S-J. 2012. Prevalence and genetic characterization of respiratory syncytial virus (RSV) in hospitalized children in Korea. Archive Virology. 157: 1039–50.

[15] Arnott A., Vong S., Sek M., Naughtin M., Beauté J., Rith S. (2013). Genetic variability of human metapneumovirus amongst an all ages population in Cambodia between 2007 and 2009. Infection. Genetics. Evolution. Journal. Molecular. Epidemioogyl, 15: 43-52.

[16] Gimferrer L., Andrés C., Campins M., Codina M, G., Rodrigo J, A., Melendo S. (2015). Circulation of a novel human respiratory syncytial virus Group B genotype during the 2014-2015 season in Catalonia (Spain). Clin. Microbiol. Infect. Off. Publ. Eur. Soc. Clin. Microbiology Infection. Disease.

[17] Ouédraogo Y., Ouédraogo R, A., Nenebi., Traoré B., Congo L., Yonli F., Kima D., Bonané P. (2016). Respiratory syncytial virus (RSV) infections at the Charles de Gaulle pediatric university hospital in Ouagadougou, Burkina Faso. Société de pathologie exotique et Lavoisier. 109: 20-25 DOI 10.1007/s13149-016-0473-6.

[18] Hamzé., Hlais S., Rachkidi J., Mallat H., Lichaa E., Zahab N. (2010). Respiratory Syncytial Virus Infections in Northern Lebanon - Prevalence during Winter 2008. Journal La Revue de Santé de la Méditerranée orientale EMHJ, Vol. 16 No. 5.

[19] Welliver R, C. (2003). Review of epidemiology and clinical risk factors for severe respiratory syncytial virus (RSV) infection. Journal Pediatrie; 143: S112-S117.

[20] Bourrillon A, Aujard Y, Costa M, Gaudelus J. 1999. Acute bronchiolitis in infants. In: Journées parisiennes de pédiatrie. Clinical evaluation and severity characteristics. Paris: Flammarion Médecine-Sciences;. p. 227-35.

[21] Young S., O'Keeffe P, T., Arnott J., Landau L, I. (1995). Lung function, airway responsiveness, and respiratory symptoms before and after bronchiolitis. Archive Disease Children, 72: 16-24.

[22] WHO. (2008). Protocol for National Sentinel Influenza Surveillance, Division of Communicable Disease Prevention and Control, West Africa Regional Office, Brazzaville.

[23] Sougue C. 2014. Surveillance Sentinelle des Syndromes Grippaux Au Burkina Faso 20102013: Investigation of Respiratory Viruses Other Than Influenza. PhD Thesis. Institut Supérieur des Sciences De la Sante, Université Polytechnique De Bobo Dioulasso, Bobo Dioulasso, Burkina Faso, 133p.

[24] Ju Yong, C., Tae H, H., Byung E, K., Chang K, K., Sang W, K., Eung-Soo H.(2006). Human Metapneumovirus Infection in Hospitalized Children with Acute Respiratory Disease in Korea. Journal Korean Medecine Science; 21: 838-42 ISSN 1011-8934.

[25] Njouom R,. Elsie L, Y., Pierre C., Astrid V., Pascal B., and Dominique R. (2012). Viral Etiology of Influenza-Like Illnesses in Cameroon, January-December 2009. Viral Etiology of ILI in Cameroon, Journal of Infectious Diseases, 2012: 206 (1) S29.

[26] Akoua-k C., Kouakou B., Kadjo H., Elia G., Koffi SP. (2007). Results of two year surveillance of flu in Abidjan, Cote d'Ivoire, *Medicale Tropicale journal*, 67 (3): 259-262.

[27] Longueville F., Hountondji Y, C., Djivo V, P., Henry S. (2013) Potential relationships between low-level acute respiratory infections and weather conditions in Benin. Environ Risque Santé, 12: 139-1350.

[28] Niang MN., Ousmane MD, Fatoumata DS, Deborah G, Hubert M-S, Kader N, Astrid V, Laurence B. 2010. Viral Etiology of Respiratory Infections in Children Under 5 Years Old Living in Tropical Rural Areas of Senegal: The EVIRA Project. Journal of Medical Virology. 82: 866-872.

[29] Stensballe LG, Devasundaram JK, Simoes EA. 2003. Respiratory syncytial virus epidemics: the ups and downs of a seasonal virus. Pediatr Infectious Diseases Journal: 22: S21-32.

[30] Bloom-Feshbach K., Alonso W. J., Charu V. (2013). Latitudinal variations in seasonal activity of influenza and respiratory syncytial virus (RSV): a global comparative review. PLoS One: 8: e54445.

[31] Giersing B, K., Karron R. A., Vekemans J., Kaslow D, C., Moorthy V, S. (2017) Meeting report: WHO consultation on respiratory syncytial virus (RSV) vaccine development, Geneva, 25-26 April 2016. Vaccine. S0264-410X (17) 30293-1.

[32] Pitzer VE, Viboud C, Alonso WJ, Wilcox T, Metcalf CJ, Steiner CA. 2015 Environmental Drivers of the Spatiotemporal Dynamics of Respiratory Syncytial Virus in the United States. PLoS Pathog 11 (1): e1004591. https://doi.org/10.1371/journal.ppat. 1004591.

[33] Weber M, W., Mulholland E, K., Greenwood B, M. (1998). Respiratory syncytial virus infection in tropical and developing countries. Tropical Medecine International Health, 3 (4): 268-80.

[34] Omer S, B., Sutanto A., Sarwo H., Linehan M., Djelantik I, G, G., Mercer D. (2008). Climatic, temporal, and geographic characteristics of respiratory syncytial virus disease in a tropical island population. Epidemiology Infectious; 136 (10): 1319-27.

[35] Chan P, W, K., Chew F, T., Tan T, N., Chua K, B., Hooi P, S. (2002). Seasonal variation in respiratory syncytial virus chest infection in the tropics. Pediatric Pulmonology; 34 (1): 47-51.

[36] Kouabenan Anderson N'Gattia. (2017). Analysis of the effects of climatological parameters on the temporal circulation dynamics of influenza viruses in Abidjan, Côte d'Ivoire, 2007-2012. PhD thesis. Université Félix Houphouet Boigny Abidjan, Côte d'Ivoire, 2017BHTN51ff. fftel-01938114f.

[37] Rachel M, Marek B, David A, Sabina G. 2019. Exhaled nitric oxide in pediatric patients with respiratory disease. Journal of Breath Research, 13 (4): 046007. doi: 10.1088/1752-7163/ab2c3d.