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Viral Acute Respiratory Infections in Central African Republic Children: Epidemiological and Clinical Aspects

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Abstract

Background: Acute respiratory infections (ARI) are recognized as an important cause of morbidity, mortality, and hospitalization among children in developing countries. **Objectives:** To identify the respiratory viruses circulating in Central African children before the SARS-COV2 pandemic and to assess the clinical manifestations. **Methodology:** This is a cross-sectional, descriptive, multicenter study, run from March 1, 2019, to March 31, 2020. Children aged 28 days to 15 year-old, with respiratory symptoms ≤10 days had been included. Nasopharyngeal swabs were taken and sent to the Institute Pasteur in Bangui (WHO National Referral Center for influenza). Virus research was done by cell and molecular culture techniques. Data were recorded and processed with Access 2019 software, then analyzed with STATA version 14 software. Chi-square test and ANOVA test were used to compare proportions at the $p < 0.05$ threshold. **Results:** Out of 659 children included during the study period, viruses were identified in 231 children, for an overall positivity rate of 35.05% (231/659). Rhinoviruses (RV) and influenza viruses were found in 66.23% and 16.88% respectively. Virus-virus co-infections were found in 10 (10/231) children (4.32%). Children under 5 years of age were more represented (78.60%). The main reasons for consultation were: fever (96.20%), cough (95.45%), runny nose (78.5%), and breathing difficulty (30.50%). ILI (Influenza-Like Illness) was found in 71.02% versus 28.98% of SARI (Severe

Acute Respiratory Infection). There was a statistically significant association between age < 5 years and severity of acute respiratory infection (p = 0.001). The outcome was known for the 122 children at the CHUPB site with a mortality rate of 17.21% (n = 21). **Conclusion:** Viral ARI is common in children in Central African Republic. Care givers should think about it in order to reduce the inappropriate prescription of antibiotics.

Keywords

Acute Respiratory Infections, Virus, Children, Central African Republic

1. Introduction

Respiratory viruses are ubiquitous and are present in all regions across the 5 continents of the world [1]. Each year, according to the World Health Organization (WHO), the influenza epidemic results in 3 to 5 million severe cases and 290,000 to 650,000 deaths worldwide [2]. ARI occurs in all age groups, with a high prevalence found in the pediatric population [3] [4] [5] [6] [7]. The prevalence of viruses in respiratory infections is difficult to estimate because they are rarely investigated routinely outside of epidemic context. Seroprevalence studies have shown that 60% - 84% of infants have significant antibodies against common respiratory viruses at birth (probably from mother). The maternal antibodies level decline to 7% - 25% in children aged 6 months to 1 year. Seroprevalence then increases to 30% - 55% in patients between 1 and 2 years of age, suggesting the acquisition of a primary infection. Approximately 38% - 70% of specimens between 2 and 5 years of age and 75% - 100% for children older than 5 years show serological evidence of exposure to respiratory viruses [1] [8] [9]. The profile of pathogens found depends on the type of respiratory infection, the age of the child and the epidemiological data of the country [10]. In the Central African Republic, the incidence of viral respiratory infections in 2014 in children under 5 years of age was 38.5% [11]. The current study following to the 2014 one aims to identify epidemiological variations of viruses circulating in children in the Central African Republic and describe clinical aspects within a period preceding and coinciding with the SARS-CoV2 pandemic.

2. Methodology

The influenza virus monitoring system is a collaborative partnership between the Ministry of Health and the Flu national reference laboratory, hosted by the Institute Pasteur in Bangui. The first sentinel sites were established in January 2008 in Bangui, the country's capital, inside the pediatric teaching hospital (CHUPB)—the only tertiary referral hospital for monitoring—and the Saint Joseph Health Center, which is a private center—run by Catholic missionaries—providing health care to very low-income populations. In 2010, monitoring was extended to public facilities of the Ministry of Health at the health district level

(Pissa health center, Boali health center, Bossembele hospital), which were selected on the basis of their accessibility, for rapid transport of case report forms and samples to the national influenza referrence laboratory. In early 2019 a pediatric emergency center managed by an independent Italian organization (AMICI Per Il Centrafrica) was added as the sixth influenza virus monotoring site in the Central African Republic.

The Institute Pasteur in Bangui—the national influenza referral laboratory—has an ABI 7500 platform (Applied Biosystems, Foster City, California, USA) with SuperScript III Platinum One-step Quantitative RT-PCR System (Invitrogen, Carlsbad, California, USA) that was used for the assays. In addition to influenza viruses, this platform detects other viruses leading to respiratory infections. In addition, the Institute Pasteur in Bangui is responsible for the monitoring supply management system, providing logistical and material support to the sentinel sites: standardized questionnaires, swabs, viral transport media, coolers and ice packs.

This study is a cross-sectional and descriptive one. It was conducted jointly on the six sentinel sites of influenza virus monitoring in the Central African Republic, from March 1, 2019, to March 31, 2020. After informed consent from their parents, children aged 28 Days to 15 years-old, presenting with fever greater than or equal to 38˚C with cough and/or other respiratory symptoms with onset within the past 10 days were included. Incomplete forms and parents' sampling rejection were the reasons for non-inclusion in the study.

Regarding the study's running, the following case definitions guided clinicians. "Influenza-like illness was defined as a temperature ≥ 38˚C and cough with onset within the past 10 days. Was considered severe acute respiratory infection a temperature ≥ 38˚C and cough with onset within the past 10 days, that required hospitalization." [12]. Following these definitions, the care givers involved in the monitoring, collected information from the parents or legal guardians of each child on the standardized questionnaire and on the survey, form including the nominative demographic characteristics; data from the interview: reasons for consultation, medical history, evolution of symptoms; data from the physical examination, paraclinical data after nasal or oropharyngeal swabbing, and the outcome of the disease (see **Appendix**). The swab from each case is placed in a tube with viral transport conditioning and stored at 2˚C - 8˚C in the sentinel site laboratory before delivery to the National Influenza Reference Laboratory within the same week, from Monday to Friday. Workshops were held quarterly to improve the monitoring system, and supervision of targeted clinical staff. The National Influenza Reference Laboratory provided weekly reports on the distribution of samples and the number of confirmed influenza cases to the Ministry of Health, sentinel sites, and WHO FluNet (http://www.who.int/influenza/gisrs_laboratory/flunet/en/) [12].

3. Laboratory Procedures

Three aliquots were taken from each sample, two of which (1 ml each) were kept

at less than 80˚C for external quality assessment (Centre for Health Protection, Department of Health, Hong Kong). The third aliquot of 140 µl was kept at 4˚C for RNA extraction with the QIAmp Viral RNA Mini Kit (QIAagen, Courtaboeuf, France) according to the manufacturer's protocol. Influenza virus was detected and subtyped by (RT-PCR) within 72 h of sample receipt [13]. All negative samples were analyzed by multiplex RT-PCR for the simultaneous detection of other respiratory viruses. The primers used are listed in Table 1.

Data from completed forms and laboratory results were recorded and processed by Access 2019 software. The diagnosis of upper or lower ARI was made on the basis of clinical symptoms for all children seen in consultation and included in the study. Children with the following clinical signs were classified as having

Table 1. Sense, anti-sense primers and double-labeled probes provided by CDC.

Primers and probes	Séquence (5' > 3')	Concentration
Primer Inf.A sense	GAC CRA TCC TGT CAC CTC TGA C	40 µM
Primer Inf.A anti-sense	AGG GCA TTY TGG ACA AAK CGT CTA	40 µM
Probes Inf.A	TGC AGT CCT CGC TCA CTG GGC ACG	10 µM
Primer A/H1 sense	AAC TAC TAC TGG ACT CTR CTK GAA	40 µM
Primer A/H1 anti-sense	CCA TTG GTG CAT TTG AGK TGA TG	40 µM
Probe A/H1	TGA YCC AAA GCC TCT ACT CAG TGC GAA AGC	10 µM
Primer A/H3 sense	AAG CAT TCC YAA TGA CAA ACC	40 µM
Primer A/H3 anti-sense	ATT GCR CCR AAT ATG CCT CTA GT	40 µM
Probe A/H3	CAG GAT CAC ATA TGG GSC CTG TCC CAG	10 µM
Primer SW A/H1 sense	GTG CTA TAA ACA CCA GCC TYC CA	40 µM
Amorce SW A/H1 anti-sens	CGG GAT ATT CCT TAA TCC TGT RGC	40 µM
Probe SW A/H1	CA GAA TAT ACA T CC RGT CAC AAT TGG ARA A	10 µM
Primer Inf.A/H5a sense	TGG AAA GTR TAA RAA ACG GAA CGT	40 µM
Primer Inf.A/H5a anti-sense	YGC TAG GGA RCT CGC CAC TG	40 µM
Probe Inf.A/H5a	TGA CTA CCC GCA G T A TTC AGA AGA AGC AAG ACT AA	10 µM
Amorce Inf.A/H5b sens	GGA ATG YCC CAA ATA TGT GAA ATC AA	40 µM
Amorce Inf.A/H5b anti-sens	CCA CTC CCC TGC TCR TTG CT	40 µM
Sonde Inf.A/H5b	TCA CCA TAC CAA CCA T CT ACC ATT CCC TGC CAT	10 µM
Amorce Inf.B sens	TCC TCA AYT CAC TCT TCG AGC G	40 µM
Amorce Inf.B anti-sens	CGG TGC TCT TGA CCA AAT TGG	40 µM
Sonde Inf.B	CCA ATT CGA GCA GCT GAA ACT GCG GTG	10 µM
Amorce RnaseP sens	AGA TTT GGA CCT GCG AGC G	40 µM
Amorce RnaseP anti-sens	GAG CGG CTG TCT CCA CAA GT	40 µM
Sonde RnaseP	TTC TGA CCT GAA GGC TCT GCG CG	10 µM

upper ARI: cough, rhinorrhea, nasal obstruction, fever and snoring. All children with cough, fever, dyspnea, chest pain, focal signs on auscultation and chest radiography were classified as having lower ARI.

To estimate age-specific disease prevalence, we categorized children by age: <5 years, 5 to <15 years [14]. Characteristic demographics of all children and positive cases by age and seasonal trends of circulating viruses were analyzed with Stata version 12 (StataCorp, Texas, USA). The chi-square test was used to assess differences in proportions and the ANOVA test to compare mean ages of children between sentinel sites. A value of $P < 0.05$ was considered statistically significant.

4. Results

A total of 659 children with ARF were included in the study, with 51.14% (n = 337) male and 48.86% (n = 322) female. The sex-ratio of 1.04. The under 5 years old were more represented 78.60% (n = 518) and 21.40% (n = 141) for the over 5 years old. The majority of samples were taken in rural areas 60.39% (n = 398). In urban areas, 39.61% (n = 261) were performed. Vaccination status was up to date in 75.72% of cases (n = 499); according to the Expanded Program of Immunization and 2.42% of children (n = 16) had traveled from one city to another in CAR during the 15 days preceding the symptomatology. The same symptomatology was found in the entourage of 7.73% (n = 51) of children. Antibiotic therapy had been instituted before sampling in 637 children (96.66%). The main reasons for consultation were: fever in 100.00% of cases (n = 659) with a duration of <5 days in 63.58% of children (n = 419), cough in 95.45% (n = 629), runny nose in 78.5% (n = 517) and breathing difficulty in 30.50% (n = 201) (See **Table 2**). The rapid malaria test was positive in 362 children (54.93%) (See **Table 3**). According to WHO global influenza standards monitoring ILI was found in 71.02% of cases (n = 468) versus 28.98% of SARI (Severe Acute Respiratory Infection) (n = 191). Of all the samples taken during the 13 months, viruses were identified in 231 children, for an overall positivity rate of 35.05% (231/659). Rhinoviruses (RV) were found in 66.23% of cases (n = 153), Influenza A and B viruses in 16.88% (n = 40), Respiratory Syncytial Viruses (RSV) in 9.09% (n = 21), Human Bocaviruses (HBoV) in 4.32% (n = 10), Human Metapneumoviruses (HMPV) in 1.73% (n = 4), Adenoviruses (ADV) in 1.29% (n = 3) and Para-influenza Viruses (PIV 1-3) in 0.43% (n = 1). Only rhinoviruses were constant throughout the year. The others had a seasonal occurrence (See **Figure 1**). Four subtypes of influenza A and B viruses were highlighted among the 33 positive cases: H1pdm 16 (48.48%), Victoria 12 (36.36%), H3N2 3 (9.09%) and Yamagata 2 (6.06%). Virus-virus co-infections were found in 10 (10/231) children or 4.32%. It was the association of influenza A and B viruses with Rhinovirus in 6 children (2.49%), Rhinovirus with Coronavirus 229E (HCoV-229E) in 0.43%, Rhinovirus with Coronavirus HKU1 (HCoV-HKU1) in 0.43%, Rhinovirus with Adenovirus in 0.43%, and Rhinovirus with Bocavirus in 0.43% (See **Figure 2**).

The hospitalization rate was 30.50% (n = 202). There was a statistically significant association between age < 5 years and severity of acute respiratory infection (p = 0.001). Rhinovirus was most associated with severity. But the difference was

Table 2. Distribution of children according to sociodemographic and anamnestic criteria.

Characteristics (N = 659)	Frequency	
	Number	Percentage
Sex		
M	337	51.14
F	322	48.86
Age in year		
< 5	322	48.86
>5	141	21.40
Study year (N = 659)		
2019	547	83.00
2020	112	17.00
Immunization status based on EIP		
No	160	24.28
Yes	499	75.72
Antibiotherapy before sample		
Yes	637	96.66
No	22	3.34
Duration of symptoms (days)		
[1 - 5[	419	63.58
[5 - 10]	240	36.42
Travel within 15 last days		
Yes	16	2.42
No	643	95.57
Presence of symptoms in surrounding		
Yes	51	7.73
No	608	92.26
Temperatures at the time of sampling		
Fever	464	70.41
Hyperthermia	170	25.79
Febricula	25	3.79
Suspicion of malaria after physical examination		
Yes	443	67.22
No	216	32.77

Table 3. Distribution of children according to malaria screening results.

Characteristics (N = 659)	Fréquence	
	Nombre	Pourcentage
Rapid test for malaria (RDT) done		
Yes	617	93.62
No	42	6.38
Malaria RDT results		
Positive	362	54.93
Négative	297	45.07
Thick drop made		
No	531	80.57
Yes	128	19.42
Results of the thick drop made		
Negative	609	92.41
Positive	50	7.59

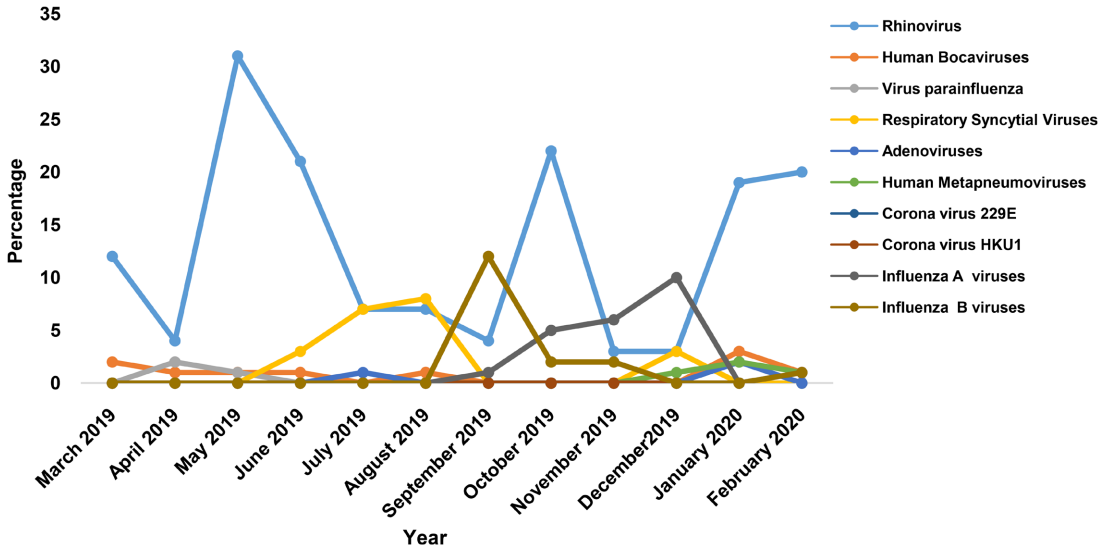

Figure 1. Distribution of viruses according to the seasons.

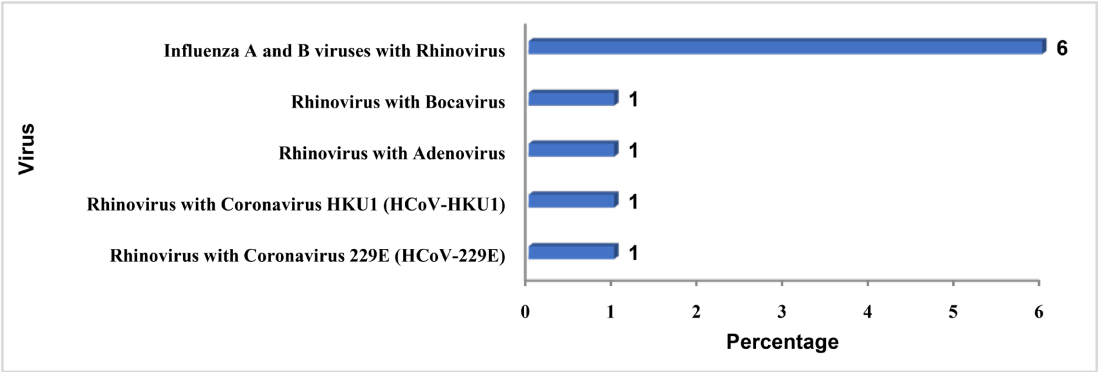

Figure 2. Distribution of children according to co-infections.

not statistically significant (P > 0.05). The outcome was known for the 122 children at CHUPB with a mortality rate of 17.21% (n = 21). Among the children who died, 95.23% (n = 20) were observed when the malaria RDT was positive P = 0.00; OR = 2000 [120 - 8323] (See Table 4).

5. Discussion

5.1. Epidemiological level

Out of 659 samples tested during the study period, at least one respiratory virus was detected in 231 children (35.05%). This prevalence is similar to that found by Bobossi *et al.* (38.5%) in 2014 in similar settings [11]; however, it is higher than Ghana's prevalence (25.7%) and lower than Zambia's one (63%) [5] [15]. The difference between these results, although concerning developing countries with a tropical climate, would be related to the viral epidemiology from one country to another, environmental factors, inclusion criteria, duration of the study, age, socioeconomic level, quality of the sample, diagnostic methods used, and the panel of viral agents tested [16]. The recent use of molecular biological methods has significantly improved the sensitivity ´of virus detection in respiratory infections [17]. The majority virus was rhinovirus (66.23%) followed by influenza A and B viruses (16.88%). Moreover, rhinovirus was found in all co-infections. The

Table 4. Distribution of viruses according to the severity of ARI by age group.

Characteristics	SARI (N, %)	ILI (N, %)	P	OR
Age (year)				
<5 (n = 190)	74 (38.94)	116 (61.06)	0.01	2.63[1.15 - 6.00]
≥5 (n = 41)	8 (19.51)	33 (80.49)		
Main Virus in children < 5 years				
Rhinovirus (n = 136)	58 (42.64)	78 (57.36)		
Virus grippaux A et B (n = 29)	10 (34.48)	19 (65.52)	0.41	1.4 [0.61 - 3.26]
Respiratory Syncytial virus (n = 17)	5 (29.42)	12 (70.58)	0.29	1.7 [0.59 - 5.34]
Other (n = 6)	1 (16.66)	5 (83.34)	0.20	3.71 [0.42 - 32.68]
Main virus in children ≥ 5 ans				
Rhinovirus (n = 22)	5 (22.72)	17 (77.28)		
Influenza A and B viruses (n = 12)	1 (8.33)	11 (91.67)	0.29	3.2 [0.33 - 31.53]
Respiratory Syncytial virus (n = 5)	1 (20)	4 (80)	0.89	1.17 [0.1 - 13.06]
Others (n = 2)	1 (50)	1 (50)	0.39	0.29 [0.01 - 5.59]
Evolution				
Rapid malaria test	**Dead**	**Favorable**		
Positive	20	1		
Negative	1	100	0.00	2000 [120 - 8323]

predominance of Rhinovirus in our study underlines its potential role in acute respiratory infections in children, and its circulation throughout the year with epidemic peaks would explain why it is mostly found in co-infection with other viruses. Viral co-circulation would be a reason for co-infections. Some have attributed viral co-detection to accidental overlap during seasonal epidemics. However, more complex mechanisms explain the onset of these co-infections. Viruses in general trigger an interferon-producing immunological mechanism that induces an antiviral state in the body [18]. It is possible that RV antagonizes interferon production, weakening the innate immune system and thereby promoting viral coinfection [18]. The ubiquitous character of rhinoviruses, their high frequency in communities, their airborne transmission, their mode of contamination by airborne vehicles [19] and their extreme resistance in the environment—giving the advantage of a long survival on an inert surface—would explain their permanent circulation. The absence of vaccination against influenza in the Central African Republic could explain the predominant place occupied by influenza viruses in our series [11]. The rate of co-infection in our series remains low compared to the series of Litwin (7%), Olofsson (10%), Mahonny (15%) and Daniel (25.5%) [11]. Did our series have few cases of immunodeficiency? We cannot answer this question because we did not investigate. Furthermore, we noted during the two monitoring analysis periods that coronavirus was already circulating in CAR in 2014. These are types 229E and HKU1 in 2014 and types 229E (HCoV-229E) and HKU1 (HCoV-HKU1) in the current round. This finding reinforces the hypothesis that African countries escaped the SARS-cov2 hecatomb because of the previous circulation of the coronavirus, which established a state of immunity.

5.2. Clinical and Therapeutic Aspects

The clinical manifestations observed are those known from upper or lower respiratory infections. Fever, present in all cases, proves the acute character of the manifestations in two children out of three. The immunocompromised or not of the children cannot be discussed here in view of what the fever suggests about the outcome of the respiratory disease: the frequent cause of immunodeficiency in the Central African Republic, mainly HIV, was not investigated and the questioning did not reveal the notion of taking immunosuppressive drugs or any clinical situation suggestive of immunodeficiency [20]. No virus seems to be specific for the topographical diagnosis; insofar as viruses with respiratory tropism initially replicate in the nose and pharynx before colonizing the lower airways according to a complex pathogenicity including the effects of the environment, the terrain and monoviral, polyviral or mixed bacterial and viral colonization [19] [21] [22] [23]. In this respect, respiratory difficulty was encountered in one child out of three in our analysis and syndromic grouping according to the WHO global influenza surveillance standards resulted in 71.02% of influenza-like illness (ILI) versus 28.98% of severe respiratory infection (SARI). Severe

clinical manifestations are more prevalent in children under 5 years of age. The susceptibility to viral respiratory infections and the predisposition to severity in this age group is reported in the literature [16] [22] [24]. The immaturity of the humoral immune system essential in the defense against respiratory viruses would be a reason [16] [25]. In addition, some authors believe that viruses such as RSV and HMPV predispose to clinical severity. In addition, certain co-infections can make the prognosis pejorative. This is the case of RSV and adenovirus [20] [22]. However, the virus-host relationship is regulated by the immune status of the patient [20]. Chorazy, went in the same direction by proving that monoviral or polyviral colonization does not influence the occurrence of severe forms of acute respiratory infections [23]. Concerning the attenuation of clinical forms, we refer to the recent work of Dee [26] where it is shown that the first colonization of rhinovirus16 induces the secretion of interferons likely to block the proliferation of SARS-Cov2. Beyond bacterial and viral co-infections, what role could malaria play? The comorbidity of malaria and SARS is very poorly documented. In the present study, the risk of death was very high in children who had a positive rapid diagnostic test (RDT) for Plasmodium falciparum. Malaria has been identified as a poor prognostic factor in Congo in children with severe respiratory infection, increasing the risk of death by 2.98 [27]. However, the lack of precision of the form of malaria (neurological or other) and the small sample size do not allow us to generalize the conclusions. The existence of co-infections (malaria-virus) may make it difficult to establish the causal link between the viruses and the respiratory symptomatology [21]. Severe forms of malaria related to severe anemia, pulmonary oedema and acidosis induce respiratory distress. This justifies the systematic performance of a malaria RDT which is easily accessible in the presence of any febrile respiratory difficulty. Moreover, as reported earlier, antibiotic therapy is instituted prior to sampling in 96.66% of children before admission. This is a real challenge in developing countries like the Central African Republic. Although immunization programs have changed the microbial epidemiology of respiratory infections in favor of a viral predominance, the inaccessibility of viral diagnostic tests and the absence of specific antiviral treatment motivate the clinician to systematically use antibiotics with the risk of resistance [19].

6. Conclusion

This analysis highlighted the virus epidemiological characteristics of children in the Central African Republic. These are: the permanent circulation of RV and the presence of influenza viruses. Clinically, children under 5 years of age are the most affected; the influenza syndrome predominates over severe acute respiratory infections with a high risk of death when associated with malaria. The review of the literature revealed the lack of research about co-morbidity with immunodeficiency or bacteria, and ultimately the limitations of the choice of anti-infective. In the future, immunization and rapid detection tests for viruses and

bacteria must be popularized and the community must be made aware of the harm of self-prescribing antibiotics if we want to protect anti-infective drugs and reducing the cost of care.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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Appendix

FEVER MONITORING **No……………………. Last name and First name:** ………………………………………………………………			
Reporting criteria: any axillary temperature (corrected) greater than or equal to **38˚C**			
Date of consultation: |__|__| / |__|__| /|__|__|__|__|		**Center:** ………………………………………………	
Care giver name: |__|__|__|__|__|__|__|__|__|__|__|__|__|__|			
Patient number in the center's registry: |__|__|__|__|__|__|			
Sex Male Female	Date of Birth: |__|__|/|__|__|/|__|__|__|__| Age: |__|__|years |__|__|months		
Address: |__|__|__|__|__|__|__|__|__|__|__|__|__|__|__|__|__|__|__|__|__|__|__|__|__|__|__|			Phone: |__|__|__|__|__|__|__|__|__|__|
SUSPICION AND DIAGNOSIS			
Axillary temperature (corrected) upon admission: |__|__|,|__| °C		**Duration since onset of fever:** |__|__| days	
Cough	**Suspected Malaria**	**RDT done:** no yes	**RDT Result:** Positive Negative
		Thick blood film done: no yes	**Thick blood film Result:** Positive Negative
	Flu Syndrome	**Case type** ILI SARI	
		Consent request for sampling no yes	
		Sampling done no yes	
		Nature of the sampling Nasal swab Throat swab Blood	Sampling Date |__|__| / |__|__| /|__|__|__|__| |__|__| / |__|__| /|__|__|__|__| |__|__| / |__|__| /|__|__|__|__|
Others Signs: (Check boxes if the sign is present)			
Sore throat	Nausea	Clinical anemia	Splenomegaly
Runny rose	Vomiting	Asthenia	Headache
Oculo-nasal catarrh	Diarrhea	Myalgia	Others…………………………………
Sub-costal retractions	Chills	Convulsion	
Dyspnea	Inability to drink or breastfeed		
Risk Factors (Check boxes if the risk factor is present)			
Asthma	Diabetes	Sick cell disease	
Heart disease	Malnutrition	Obesity	
Travel within the last 15 days	no	yes	if yes, specify location: ……………………
Presence of other people with the same symptomatology surrounding: no yes			
Treatment before admission no yes (Check the box if treatment prescribed)			
Antibiotics	Antimalarias	Antihistamines	Antipyretics
Bronchodilators,	Others………………………………………………………………..		
SARI Diagnosis (Choose one option)			
Isolated upper respiratory disease Lower respiratory disease with wheezing Exacerbation of asthma			

Continued

Upper and lower respiratory diseases Bronchiolitis Other……	
ILI Diagnosis (Choose one option)	
Yes No	
Outcome	
Cured(e) Alive dead if yes date of death |__|__| / |__|__| /|__|__|__|__|	
Number of days of hospitalization: |__|__|	
Date of sampling reception: |__|__| / |__|__| /|__|__|__|__| Area District Year Case number	**Num of tube:** |__|__|__| |__|__|__| |__|__| |__|__|__|__|__|
BIOLOGIC DIAGNOSIS	
Flu viruses: Yes ☐ No ☐ **If, yes, specify types**: A ☐ B ☐ **Sub-types:** ……	**Other viruses:** Yes ☐ No ☐ If yes, specify:……