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Epidemiological, Clinical and Virological Profiles of Influenza Infection in the Democratic Republic of the Congo, from 2009 to 2018

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Abstract

Background: To better understand the epidemiological characteristic of influenza infection, the Democratic Republic of Congo set up the sentinel influenza surveillance system in 2007 with eleven health facilities. Oral and nasopharyngeal specimens were sampled from outpatients with influenza-like illness (ILI) and inpatients with severe acute respiratory illness (SARI) using case definitions. Those specimens were shipped to the Influenza National Laboratory for testing with the real-time reverse-transcription polymerase chain reaction. This study aimed to describe ILI and SARI patients' epidemiological, clinical, and virological profiles. **Material and Method:** We conducted a cross-sectional study based on a documentary review of suspected notified influenza cases from January 2009 to December 2018. As variables, we exploited sex, age, symptoms, sentinel site of provenance, patient category, viral type and subtype identified, and period of health facility visit. **Results:** Of 18,461 notified cases, 1795 (9.7%) were positive for the Influenza virus, among them; 53.1% of patients under five years old; 68% of type A virus, 31.5% of type B; 21% of SARI positive vs. 79% for ILI positive cases. The majority of cases occurred during the rainy season. **Conclusion:** The results of this study contribute to a better understanding of the influenza infection in the Democratic Republic of Congo.

Keywords

Sentinel Surveillance, Influenza, DRC

1. Introduction

Following the emergence in 1997, of a Highly Pathogenic Avian Virus A/H5N1, in Asia that spread in Europe in 2005 and Africa in 2006 (Egypt, Nigeria and Cameroon), infecting both poultry and humans [1], some African countries like Kenya [2], Tanzania [3], Rwanda [4], Nigeria [5], Senegal [6] and Zambia [7], had set up influenza surveillance systems with WHO and CDC/Atlanta [8] support.

Since 2007, the Democratic Republic of Congo (DRCongo) has implemented an influenza sentinel surveillance network with the following objectives: 1) to detect new influenza strains with a potential pandemic; 2) to determine epidemiological traits of influenza and other viral respiratory diseases; 3) to monitor the trend of deaths imputable to severe acute respiratory illness (SARI) patients; 4) to determine the proportion of positive influenza cases amid inpatients and outpatients; 5) to collect meaningful epidemiological, virological and socio-economic data for estimating the influenza burden in the DRCongo.

Based on sentinel surveillance data, the prevalence of influenza infection was respectively estimated to be 1205 and 48.5 for ILI (Influenza-like Illness) and SARI confirmed patients per 100,000 inhabitants (national and provincial burden) in 2016 [9]. About mortality, the case-fatality proportion was estimated to be 1.2% of SARI positive cases [10].

This study aimed to determine influenza epidemiological, clinical, and virological profiles of patients who attended sentinel sites in DRCongo between 2009 and 2018.

2. Material and Method

1) Framework of the study

Our study focused on the eleven sentinel surveillance sites and the national influenza laboratory in the DRCongo, between January 2009 and December 2018. These sites were located both in the capital Kinshasa and in five DRCongo provinces and were also geographically representative, financially accessible, staffed with qualified health care providers, equipped with a cold chain and regularly supplied for sample collection. Two sites were medical clinics intended for ILI outpatients and nine were hospitals for both inpatients and outpatients. In Kinshasa, the following health facilities where selected: Kinshasa provincial general hospital, Kalembelembe pediatric hospital, Kingasani hospital Centre, Boyambi and RVA medical clinics. In provinces, they were: Kinkanda and Matadi Referral General Hospital in Kongo-Central, Kenya and Kisanga Referral General Hospitals in Haut-_Katanga, Charité Maternelle hospital in Nord-Kivu, and the Dipumba Referral General Hospitals in Kasai-Oriental, Boyambi and RVA medical Clinics were ILI sites, while other were ILI and SARI sites.

2) Type of study

We conducted a cross-sectional with secondary data of notified suspected influenza cases, tested with RT-PCR, from January 2009 through December 2018.

3) Study population

The study population was constituted of patients who had attended the eleven sentinel sites between January 1, 2009, and December 31, 2018 suffering for respiratory infection. As eligible case in this study, we included any inpatient or outpatient who had visited a sentinel site for respiratory issue, fulfilled ILI or SARI case definition, undergone nasopharyngeal and/or oropharyngeal sampling and tested with RT-PCR. On the other hand, we excluded from this study any other patients who has not met these requirements.

4) Sampling technique

We conducted an exhaustive sampling to obtain a large sample size for increasing the representativeness of the study population, and consequently reducing the selection bias. Of 380,867 patients who had visited the 11 sentinel sites for respiratory issues, 32,708 were ILI and SARI notified cases, among them 19,622 sampled cases. A total of 18,461 were tested with RT-PCR amid sampled cases. Those patients who performed the RT-PCR constituted our size sample, as shown in Figure 1. As statistical unit, we considered any patient who ultimately performed RT-PCR testing, from January 1, 2009, through December 31.

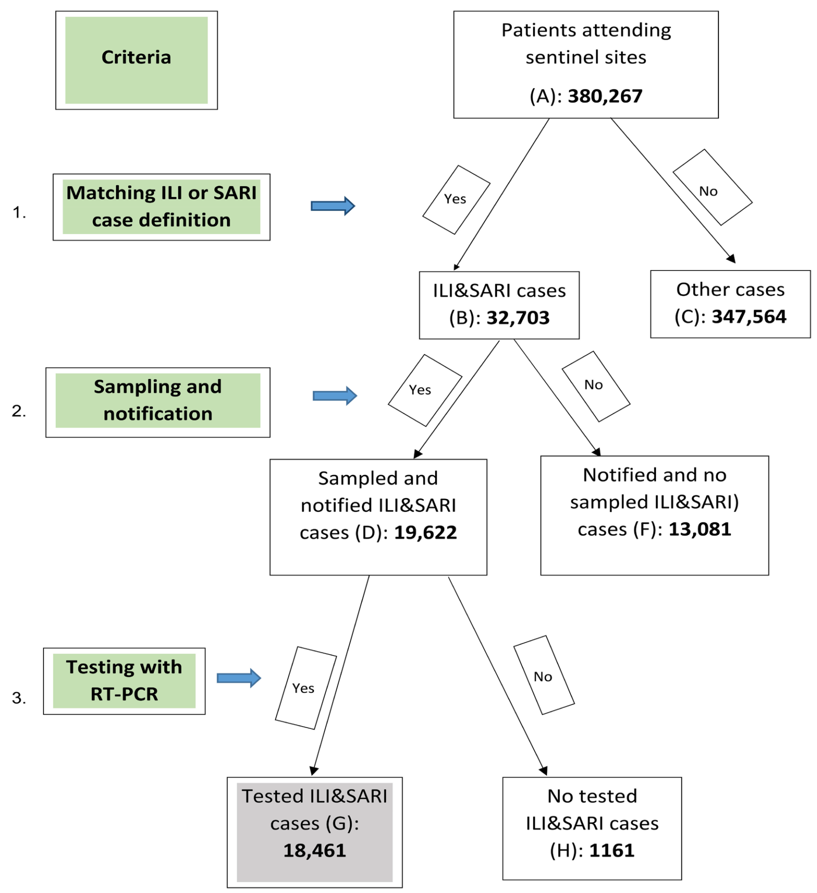

Figure 1. Study design.

5) Data collection

We extracted data from the database of notification forms sent by the sentinel sites to the national influenza laboratory. We had also recourse to the surveillance system's database of the ministry of health. All data were collected between December 2021 and March 2022 using EPIINFO.7.

6) Data processing and analysis

We processed and analysed variables like sex, age, provenance site, patient category (ILI or SARI), identified viral type and subtype and the period of illness. For that, we used Excel, Stata 16.0 for calculating frequencies, percentages as well as measures of association by using bivariate analysis, with p-value and brut odd ratio measures. For quantitative variable like age, we calculated the median as a measure of central tendency.

7) Ethical considerations

We required and obtained the IRB approval.

3. Results

Sex Analysis

Of 18461 samples tested, 1795 (9.7%) were positive, among them 1273 (79%) were ILI and 522 (21%) SARI. Positive men were 927 (51.6%), while positive women were 868 (48.4%). By Comparing positive ILI cases to positive SARI cases according to sex, men represented 51% and 54%, respectively, while 49% of positive women were positive for ILI and 46% for SARI. These differences were not statistically significant. The p-value was greater than 0.05 for both situations, as shown in **Table 1**.

Analysis by age

The median age of patients was four years old (range 4 - 98). By considering the age groups according to the positive cases (n = 1795), the age group < 2 years ranked first with a total of 560 cases (31.1%) of positive cases, while the age group age ≥ 65 years ranked last with 27 cases (1.5%). There were 14 cases with missing age (0.8%).

Regarding positive cases, 5 - 14 years old age group ranks first with 24% of ILI cases, while for SARI the age group < 2 years old came first with 52%. Furthermore children under five years old pilling up <2 years and 0 - 4 years old totalise 969 (54%) cases. An association between age and positive influenza cases was found in 2 - 4 and 5 - 14 years old age groups with a p-value < 0.05.

Analysis according to disease symptoms.

In this study, we considered frequently encountered symptoms in ILI and SARI patients, like fever, cough, sore throat, cold, headache, and dyspnoea. Regarding ILI patients, **Table 1** shows that cough came first (98%), followed by colds (96%), fever (84%), dyspnoea (58%), sore throat (36%), and finally headaches (24%). For SARI patients, cough was still kept the first rank (98%), followed by fever (93%), dyspnoea (90%), and colds (89%). Sore throat and headaches were less frequent symptoms, respectively, with 64 and 17%. For both ILI

Table 1. Socio-demographic and clinical characteristics of enrolled patients.

Type of patients	ILI (n = 11,659)				SARI (n = 6802)			
Analysis results	Positive influenza	Negative influenza	p-value	GOLD 95%	Influenza positive	Influenza negative	p-value	95% GOLD
Effective (%)	1273 (100)	10,386 (100)			522 (100)	6280 (100)		
Sex								
Male	647 (51)	5065 (49)	0.17	1.1 (1 - 1.2)	280 (54)	3203 (51)	0.255	1.1 (0.9 - 1.3)
Female	626 (49)	5321 (51)		1	242 (46)	3077 (49)		1
Age								
Median age	4 (0 - 84)	4 (0 - 98)			4 (0 - 86)	4 (0 - 97)		
<2 years	290 (23)	2743 (26)	0.055	1.7 (1 - 3.1)	270 (52)	3311 (53)	0.290	1.4 (0.8 - 2.8)
2 - 4 years	292 (23)	1950 (19)	0.000	2.4 (1.4 - 44)	117 (22)	844 (13)	0.003	2.4 (1.3 - 4.9)
5 - 14 years old	301 (24)	1257 (12)	0.000	3.1 (1.8 - 5.6)	52 (10)	425 (7)	0.023	2.1 (1.1 - 4.5)
15 - 39 years old	249 (19)	2472 (24)	0.104	1.6 (0.9 - 2.9)	36 (7)	840 (14)	0.361	0.47 (0.4 - 1.6)
40 - 64 years old	115 (9)	1681 (16)	0.451	1.1 (0.6 - 2.0)	32 (6)	638 (10)	0.720	0.89 (0.4 - 1.9)
≥65 years old	15 (1)	238 (2)		1	12 (2)	208 (3)		1
Unknown	11 (1)	45 (0)			3 (1)	14 (0)		
Symptoms								
Cough								
Yes	1238 (97)	10,137 (97)	0.376	1.6 (0.7 - 4.7)	515 (98)	6157 (98)	0.474	0.68 (0.2 - 3.6)
No	6 (1)	78 (1)		1	3 (1)	25 (0)		1
Unknown	29 (2)	171 (2)			4 (1)	98 (2)		
Fever								
>38˚C	1071 (84)	8667 (83)	0.000	1.6 (1.3 - 2.0)	484 (93)	5845 (93)	0.178	1.5 (0.8 - 2.8)
<38˚C	164 (13)	1353 (13)		1	13 (5)	236 (4)		1
Unknown	38 (3)	366 (4)			25 (2)	199 (3)		
Sore throat								
Yes	459 (36)	4947 (48)	0.000	0.7 (06 - 08)	296 (57)	3855 (61)	0.093	0.8 (0.7 - 1.0)
No	449 (35)	3277 (32)		1	135 (26)	1458 (23)		1
Unknown	365 (29)	2162 (20)			91 (17)	967 (16)		
Dyspnoea								
Yes	58 (5)	586 (6)		1	449 (86)	5612 (90)	0.68	0.9 (0.6 - 1.4)
No	820 (64)	7176 (69)	0.343	1.2 (0.9 - 1.6)	29 (6)	334 (5)		1
Unknown	395 (31)	2624 (25)			44 (8)	334 (5)		
Headache								
Yes	304 (24)	2998 (29)		1	58 (11)	1074 (17)		1
No	620 (49)	5149 (50)	0.021	1.2 (1.02 - 1.4)	347 (67)	4024 (64)	0.011	1.6 (1.2 - 2.2)
Unknown	349 (27)	2239 (21)			117 (22)	1182 (19)		
Common cold								
Yes	1218 (96)	9843 (95)	0.055	1.5 (1 - 2.4)	489 (94)	5587 (89)	0.015	1.7 (11 - 33)
No	24 (2)	294 (3)		1	16 (3)	341 (5)		1
Unknown	31 (2)	249 (2)			17 (3)	352 (6)		

and SARI patients an association between fever ≥ 38˚C, sore throat, absence of headache, and positive Influenza was found with a p-value < 0.05. On the other hand the same association was established for SARI patients, with also cold in addition.

Analysis according to age and the viral type and subtypes.

Regarding the repartition of positive cases (n = 1795) according to age groups and to viral type and subtype, the results were illustrated in Table 2. This shows that there were 1221 positives cases (68%) of type A virus, 566 cases (31.5%) of type B virus, and 8 co-infected cases A&B types. Among the 1221 positive cases of type A virus, the A(H3N2) subtype accounted for 595 cases (46.6%), followed by the A(HIN1)pdm09 (pandemic) subtype with 548 cases (44.6%), and the A(H1N1)s (seasonal) subtype with 11 cases (0.9%). In addition, 8 co-infected A(H3N2) and A(H1N1)pdm09 cases (0.3%) and 92 no subtyped cases (7.5%) were reported. This table also shows that by calculating the percentages of each type by age group, the type B had respectively 33.2% and 23.3% of cases in <2 years and 2 - 4 years age groups vs. 30% and 22.6% for the type A in the same age groups.

Analysis of positive case by provenance and category of patient

Of 1795 positive cases, 1273 were ILI (71%), and 522 SARI (29%). Considering the ILI-positive cases, Boyambi medical clinic occupied the first place with 22.5%, followed by RVA medical clinic, which totalled 21.8%. For SARI positive cases, the first place went to Kalembelembe paediatric hospital with 43.8%, followed by Kingasani hospital with 22.0%, as shown in Figure 2

Analysis by quarters and years

As regard to positive cases, the first quarter occupied the ranking top with 35.4% of cases, followed by the second quarter, with 30.4%, the fourth quarter with 29.8%, and finally, the third quarter came last with 4.5% of cases, as shown in Table 3.

Table 2. Distribution of positive cases according to age groups and viral types and subtypes.

	A(H1N1) pdm09	A(H1N1)s	A(H3N2)	A(H3N2 & H1N1)p	Not subtyped	Total Type A	% Type A	Type A&B	% Type A&B	B-Type	% Type B	Total A, A & B, B
0 < 2 years	161	5	172	2	31	**371**	30.4	1	12.5	188	33.2	**560**
2 - 4 years	115	1	140	2	17	**275**	22.5	2	25.0	132	23.3	**409**
5 - 14 years old	117	1	94	0	19	**231**	18.9	3	37.5	119	21	**353**
15 - 39 years old	104	3	83	0	15	**205**	16.8	2	25.0	78	13.8	**285**
40 - 64 years old	40	1	63	0	6	**110**	9	0	0.0	37	6.5	**147**
≥65 years old	4	0	10	0	2	**16**	1.3	0	0.0	11	2	**27**
Unknown	4	0	7	0	2	**13**	1.1	0	0.0	1	0.2	**14**
Total	545	11	569	4	92	**1221**	100	8	100.0	**566**	100.0	**1795**

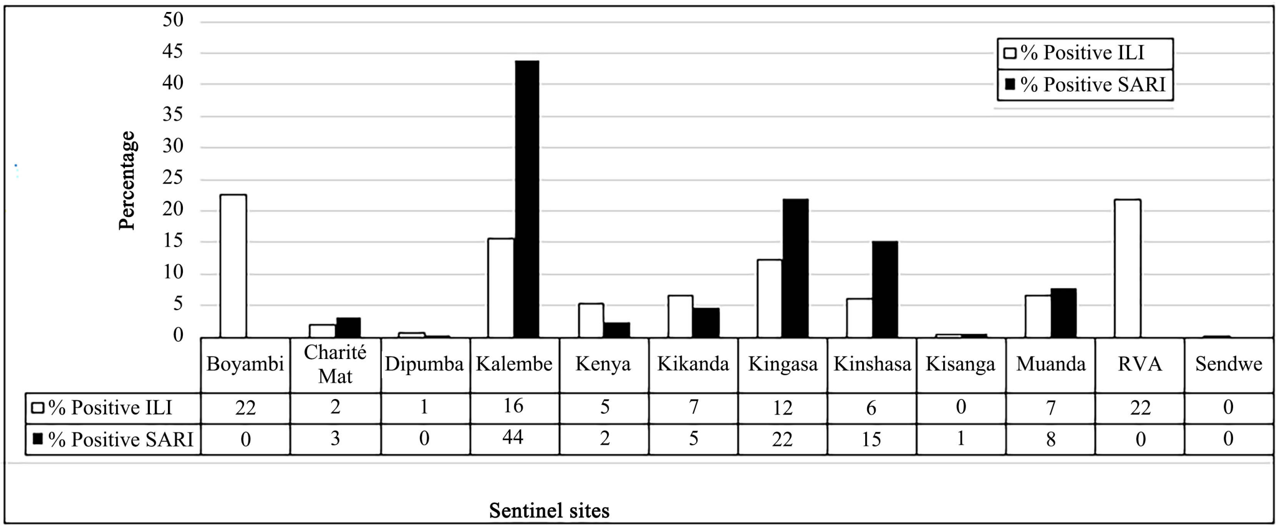

Figure 2. Percentage of positive ILI and SARI case of influenza viruses in sentinel sites.

Table 3. Distribution of positive cases per quarter and per year according to the types and subtypes of the influenza virus.

Period	A(H1N1)pdm09	A(H1N1)s	A(H3N2)	A(H3N2) & A(H1N1) pdm09	Not subtyped	Type A & B	B Type	Total positive	% positive
Trimester									
Quarter 1	114	10	313	0	1	29	168	635	35.4
Quarter 2	101	1	117	1	5	19	301	545	30.4
Trimester 3	17	0	24	0	1	3	35	80	4.5
Quarter 4	313	0	115	3	1	41	62	535	29.8
Total quarters	**545**	**11**	**569**	**4**	**8**	**92**	**566**	**1795**	**100**
Year									
2009	176*	11	39	3	24	0	18	271	15.1
2010	11	0	77	0	2	3	148*	241	13.4
2011	40	0	138*	0	19	1	38	236	13.1
2012	67*	0	31	0	5	1	11	115	6.4
2013	35	0	101	0	8	1	107*	252	14
2014	12	0	105*	0	27	0	101	245	13.6
2015	110*	0	42	1	4	2	69	228	12.7
2016	45*	0	15	0	3	0	35	98	5.5
2017	43*	0	11	0	0	0	23	77	4.3
2018	6	0	10	0	0	0	16*	32	1.8
Total years	**545**	**11**	**569**	**4**	**92**	**8**	**566**	**1795**	**100**

* Predominant viral strain during the year.

By comparing the frequency of viral strains in circulation, the A(H3N2) subtype was more frequent in the year's first quarter, whereas the type B was predominant in the second and third quarters, while the A(H1N1)pdm09 subtype was more important in the fourth quarter.

Concerning, the distribution by year, the size of the annual confirmed influenza cases varied between 32 and 271 with a median of 232 as illustrated in **Table 3**. This table shows that 2009 ranked first with 15.1%, followed by 2013 with 14%, then 2014 with 13.6%, and in the last position, 2018 with 1.8%. In addition, the subtype A(H1N1)pdm09 was the most frequent strain in 2009, 2012, 2015, 2016, and 2017. Nevertheless, the A(H3N2) strain was predominant in 2011, 2014, and 2018, while the type B was dominant in 2010, 2013, and 2018. From 2010, the seasonal A(H1N1)s strain disappeared.

About the circulation of the predominant viral strains, we have observed over the course of ten years the following pattern:
A(H1N1)pdm09-B-A(H3N2)-A(H1N1)pdm09 cycle.

4. Discussion

1) *Sense of study*

Our study aimed to address the epidemiological, clinical and virological characteristics of people affected by seasonal influenza who visited sentinel surveillance sites from 2009 to 2018. For that, we should answer the following questions: Whom were these people affected by the flu? What were the clinical symptoms that they presented? Where did they live? What types and subtypes of the virus were they infected?

2) *Statement of main results*

The results of our study showed that: influenza accounted for 9.8% of other severe acute respiratory infections; children under five year old were the most affected by the flu in the DRCongo; symptoms such as fever ≥ 38˚C, sore throat, absence of headache, were associated with influenza infection; viral strains A(H3N2), A(H1N1)pdm09 and B circulated each year concomitantly, but in different proportions; the circulation pattern of viral strains was A(H1N1)-B-A(H3N2)-A(H1N1)pdm09; influenza outbreaks were observed more in the first, second and fourth quarters of the year; influenza season has two waves(the first occurs in the fourth quarter, and the second in the second quarter).

3) *Discussion of material differences in results*

Our study showed that positive cases of the influenza virus accounted for 51.6% for men and 48.4% for women, respectively. This difference is not significant, $p > 0.05$. This result differs from some studies where female sex was a risk factor [11] [12] [13] but is similar to those found in many African countries [4] [5].

Concerning age, the results of our study showed that the age groups of <2 years and 2 - 4 years represented approximately 66% of SARI positive cases and 46% of ILI positive cases, hence the interest in direct priority interventions in the fight against influenza to this target group like vaccination and case management. KATZ *et al.* in 2009 also found in Kenya similar results, in a study on the findings of the first six years of influenza sentinel surveillance. According to this study, the age group under five years and specifically that under two years was the most affected, with 33% of cases [14]. Several African studies had also shown the heavy burden children under five carry on morbidity and mortality from influenza [2]-[9] [15] [16]. In addition, the absence of data on the follow-up of complications and mortality by age group on the notification forms did not allow us to determine the age group at risk of complications and death.

Regarding the distribution of confirmed positive cases according to age groups and the viral type and subtype, the results of our studies showed that there were more positive cases of the A (H3N2) viral subtype in <2 years, 2 - 4 years age groups, and beyond 40 years than positive cases for the viral subtype A(H1N1)pdm09. On the other hand, the A(H1N1)pdm09 subtype was predominant in of 5 - 14 and 15 - 39 years age groups.

In Zambia, Theo *et al.* in 2009 had obtained similar results that showed children under five years old were more affected by the viral subtype A (H3N2) and type B. Nevertheless, the difference was found in the slices affected by A(H1N1)pdm09 which in Zambia [7] concerned people aged 5 to 24 years old, whereas in our study, the infected people were between 5 and 39 years old. Studies conducted by Dalhatu in 2010 in Nigeria [5] and Homaira in 2009 in Bangladesh [17] showed that the A(H1N1)pdm09 subtype was not significant below five years of age. However, the results obtained by these two researchers differ in the age group of people affected by this subtype. The first found that the A(H1N1)pdm09 subtype was important between 5 and 17 years and greater than 65 years. The second instead found the age range between 5 and 55 years. The difference in results between these two researchers is explained, among other things, by the difference in the age groups used.

Compared to the symptoms manifested by patients, the cough was not associated with the Influenza virus infection, which is considered one of the main symptoms of this infection. This result is different from those found in many studies [18] [19] [20]. In addition, headaches were inversely associated with influenza infection. This finding differs to that reported by Barakat *et al.* in 2011, and Hirves *et al.* in 2012 [16] [18]. The reason would be that cough should be accompanied by fever to be a predictor of influenza infection.

Regarding positive cases according to their category and provenance, our study found that ILI cases represented 79% and SARI cases, 21%. Three assumptions could explain this difference. The first is the presence of two sentinel sites which only collected ILI cases (RVA and Boyambi medical clinic). The second would be the low sensitivity of the SARI case definition compared to the ILI case [21], and the third stems from the second would be the often late arrival of SARI cases at the hospital beyond the time required for the sample.

As for the provenance of the patients, Kalembelembe paediatric hospital recorded 43.8% of SARI cases. We believe this result is justified insofar as this site is a paediatric reference hospital at the provincial level and therefore receives severe cases, including SARI cases.

Our study found that the third quarter (July, August and September) had fewer positive cases of the Influenza virus than other quarters. This period could therefore conducive for the vaccination campaign. As a possible explanation, this quarter coincides with the dry season, while the first quarter (January, February and March) and the fourth quarter (October, November and December) experience outbreaks during the rainy season. Other countries with tropical climates in Africa and Asia, like Kenya, Rwanda, Thailand, Singapore and Bangladesh [22]-[28] had experienced influenza epidemics during the rainy season.

Compared to the circulation of viral types and subtypes, we found that subtype A(H1N1)pdm09 was the most frequent strain in 2009, 2012, 2015, 2016 and 2017. On the other hand, the H3N2 strain was predominant in 2011, 2014 and 2018, while type B was more frequent in 2010, 2013 and 2018. Unlike the A(H1N1)pdm9 virus was predominant in DRCONGO in 2009, West Africa was under the grip of the A(H3N2) virus during the same period. When the type B virus was predominant in the DRCongo and southern Africa in 2010, West Africa was mainly affected by the A(H1N1)p subtype [29]. This situation shows that influenza viruses circulate differently from one region to another. Some studies have incriminated temperature and humidity as factors of variability [30] [31] [32] [33] [34]. These factors differ according to geographical areas.

Furthermore, our study showed a pattern of viral circulation in the form of a loop in the following order A(H1N1)pdm09-BA-(H3N2)-A(H1N1)pdm09. In Cameroon, a study conducted by Njoum in 2014 found the same pattern between 2009 and 2013. Therefore, this circulation pattern would constitute a research hypothesis that could target several countries.

In addition, we have noted a decrease of reported cases in 2016, 2017 and 2018. This statement was due to funding reduction for the surveillance system. Our study also showed that 2009 had more cases than other years due to the A(H1N1)pdm09 pandemic.

4) Limit of the study

Regarding the clinical characteristics, we could not obtain data on the evolution of hospitalised patients. For example, we would have liked to know how many hospitalised patients were healed and how many died.

5. Conclusions

The human infection with influenza virus represented 9.8% of acute respiratory infections in the DRCongo. This illness rages during the rainy session and most often affects children, particularly those under five years old, with a predominance of SARI cases compared to ILI cases. This study also showed that the A(H1N1)pdm09, H3N2 and type B subtypes were circulating concomitantly. According to the annual dominant strains, the human influenza virus circulates in a sequence of A(H1N1)pdm09-B-A(H3N2)-A(H1N1)pdm09 in loop form. The A(H1N1)pdm09 strain has wiped out the A(H1N1)s (seasonal) strain. This pandemic virus, assorted from three strains (human, poultry, and pig), is sufficient proof that influenza remains a threat to public health against which the sentinel surveillance system should be strengthened within one health framework.

What is known about this subject?

- Children under 5 are the most affected by influenza infection;
- Influenza infection is associated with rainfall season;
- The strains circulating in the DRCONGO are A(H1N1)p, H3N2 and type B.

What does your study bring new?

- In the viral circulation, there would be an alternation according to the dominant strains of the order…A(H1N1)p-BA(H3N2)-A(H1N1)pdm09;
- The DRCongo influenza season has two waves: The first occurs in the fourth quarter, and the second in the second quarter.

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Conflicts of Interest

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

References

[1] Lai, S., Qin, Y., Cowling, B.J., Ren, X., Wardrop, N.A., Gilbert, M.A., *et al.* (2016) Global Epidemiology of Avian Influenza A H5N1 Virus Infection in Humans, 1997-2015: A Systematic Review of Individual Case Data. *The Lancet Infectious Diseases*, **16**, e108-e118. https://doi.org/10.1016/S1473-3099(16)00153-5

[2] Katz, M.A., Muthoka, P., Emukule, G.O., Kalani, R., Djunguna, H., *et al.* (2014) Results from the First Six Years of National Sentinel Surveillance for Influenza in Kenya, July 2007-June 2013. *PLOS ONE*, **9**, e98615. https://doi.org/10.1371/journal.pone.0098615

[3] Mmbaga, V.M., Mwasekaga, M.J., Mmbuji, P., Matonya, M., Mwafulango, A., Moshi, S., *et al.* (2012) Results from the First 30 Months of National Sentinel Surveillance for Influenza in Tanzania 2008-2010. *The Journal of Infectious Diseases*, **206**, 80-86. https://doi.org/10.1093/infdis/jis540

[4] Nyatanyi, T., Nkunda, R., Rukelibuga, J., Peleka, R., Muhipundu, M.A., Kabeja, A., *et al.* (2012) Sentinel Influenza Surveillance in Rwanda, 2008-2010. *The Journal of Infectious Diseases*, **206**, 74-92. https://doi.org/10.1093/infdis/jis574

[5] Dalhatu, I.T., Medina-Marino, A., Olsen, S., Hwang, I., Gubio, A.B., Ekanam, E.E., *et al.* (2012) Influenza Viruses in Nigeria, 2009-2010: Results from the First 17 Months of a National Influenza Sentinel Surveillance System. *The Journal of Infectious Diseases*, **206**, S121-S128. https://doi.org/10.1093/infdis/jis584

[6] Dia, N., Dienne Sarr, F., Thiam, D., Faye Sarr, T., *et al.* (2014) Influenza-Like Illnesses in Senegal: Not Only Focus on Influenza Viruses. *PLOS ONE*, **9**, e93227. https://doi.org/10.1371/journal.pone.0093227

[7] Theo, A., Liwewe, M., Ndumba, I., Mupila, Z., Tambatamba, B., Mutembo, C., *et al.* (2012) Influenza Surveillance in Zambia, 2008-2009. *The Journal of Infectious Diseases*, **206**, S173-S177. https://doi.org/10.1093/infdis/jis599

[8] Steffen, C., Debellut, F. and Gessner, B.D. (2012) Improving Influenza Surveillance in Sub-Saharan Africa. *Bulletin of the World Health Organization*, **90**, 301-305. https://scholar.google.fr/scholar?cluster=16263510640599714153&hl=fr&as_sdt=0,5#

[9] Babakazo, P., Lubula, L., Disasuani, W., Manya, L.K., *et al.* (2018) The National and Provincial Burden of Medically Attended Influenza-Associated Influenza-Like Illness and Severe Acute Respiratory Illness in the Democratic Republic of Congo, 2013-2015. *Influenza and Other Respiratory Viruses*, **12**, 695-705. https://doi.org/10.1111/irv.12601

[10] McMorrow, M.L., Wemakoy, E.O., Tshilobo, J.K., Emukule, G.O., Mott, J.A., Njuguna, H., *et al.* (2015) Severe Acute Respiratory Illness Deaths in Sub-Saharan Africa and the Role of Influenza: A Case Series from 8 Countries. *The Journal of Infectious Diseases*, **212**, 853-860. https://doi.org/10.1093/infdis/jiv100

[11] Klein, S.L., Hodgson, S. and Andrea, R.P. (2012) Mechanisms of Sex Disparities in Influenza Pathogenesis. *Journal of Leukocyte Biology*, **92**, 67-73. https://doi.org/10.1189/jlb.0811427

[12] Giurgea, L.T., Cervantes-Medina, A., Walters, K.A., Schelter, K., Han, A., Czajkowski, L., *et al.* (2021) Sex Differences in Influenza: The Challenge Study Experience. *The Journal of Infectious Diseases*, **225**, 715-722. https://doi.org/10.1093/infdis/jiab422

[13] Peretz, J., Hall, O.J. and Klein, S.L. (2015) Sex Differences in Influenza Virus Infection, Vaccination, and Therapies. In: Klein, S.L. and Roberts, C.W., Eds., *Sex and Gender Differences in Infection and Treatments for Infectious Diseases*, Springer, Cham, 183-210. https://link.springer.com/chapter/10.1007/978-3-319-16438-0_6

[14] Katz, M.A. Lebo, E., Emukule, G., Njuguna, H.N., Aura, B., Cosmas, A., *et al.* (2012) Epidemiology, Seasonality, and Burden of Influenza and Influenza-Like Illness in Urban and Rural Kenya, 2007-2010. *The Journal of Infectious Diseases*, **206**, S53-S60. https://doi.org/10.1093/infdis/jis530

[15] Nair, H., Brooks, W.A., Katz, M., Roca, J.A., Madhu, S., Simmeman, J.M., *et al.* (2011) Global Burden of Respiratory Infections Due to Seasonal Influenza in Young Children: A Systematic Review and Meta-Analysis. *The Lancet*, **378**, 1917-1930. https://doi.org/10.1016/S0140-6736(11)61051-9

[16] Barakat, A., Ihazmad, H., Benkaroum, S., Cherkaoui, I., Benmamoun, A., Youbi, M., *et al.* (2011) Influenza Surveillance among Outpatients and Inpatients in Morocco, 1996-2009. *PLOS ONE*, **6**, e24579. https://doi.org/10.1371/journal.pone.0024579

[17] Homaira, N., Luby, S.P., Alamgir, A.S., Islam, K., Paul, R., Abedin, J., *et al.* (2012) Influenza-Associated Mortality in 2009 in Four Sentinel Sites in Bangladesh. *Bulletin of the World Health Organization*, **90**, 272-278. https://www.scielosp.org/pdf/bwho/v90n4/v90n4a10.pdf

[18] Hirve, S., Chadha, M., Lele, P., Lefond, K., Daeshatwar, A., *et al.* (2012) Performance of Case Definitions Used for Influenza Surveillance among Hospitalised Patients in a Rural Area of India. *Bulletin of the World Health Organization*, **90**, 804-812. https://doi.org/10.2471/BLT.12.108837

[19] Kasper, M.R., Wierzba, T.F., Sovann, L., Blair, P.J. and Putman, S.D. (2010) Evaluation of an Influenza-Like Illness Case Definition in the Diagnosis of Influenza among Patients with Acute Febrile Illness in Cambodia. *BMC Infectious Diseases*, **10**, Article No. 320.

https://bmcinfectdis.biomedcentral.com/articles/10.1186/1471-2334-10-320

[20] Woolpert, T., Brodine, S., Lemus, H., Waalen, J., Blair, P. and Faix, D. (2012) Determination of Clinical and Demographic Predictors of Laboratory-Confirmed Influenza with Subtype Analysis. *BMC Infectious Diseases*, **12**, Article No. 129. https://bmcinfectdis.biomedcentral.com/articles/10.1186/1471-2334-12-129

[21] Murray, E.L., Khagayi, S., Ope, M., Biggio, G., Ochala, R., Muthoka, P., *et al.* (2013) What Are the Most Sensitive and Specific Signs and Symptom Combinations for Influenza in Patients Hospitalised with Acute Respiratory Illness? Results from Western Kenya, January 2007-July 2010. *Epidemiology and Infection*, **141**, 212-222. https://doi.org/10.1017/S095026881200043X

[22] Finkeman, B.S., Viboud, C., Koelle, K., Ferrari, M.J., Barthi, N., Grenfell, B., *et al.* (2007) Global Patterns in Seasonal Activity of Influenza A/H3N2, A/H1N1, and B from 1997 to 2005: Viral Coexistence and Latitudinal Gradients. *PLOS ONE*, **2**, e1296. https://doi.org/10.1371/journal.pone.0001296

[23] Gachara, G., Ngeranwa, J., Magana, J.M. and Simwa, J. (2006) Influenza Virus Strains in Nairobi, Kenya. *Journal of Clinical Virology*, **35**, 117-118. https://doi.org/10.1016/j.jcv.2005.10.004

[24] Simmerman, J.M., Chittaganpich, M.L., Wango, P. and Lifumo, S. (2009) Incidence, Seasonality and Mortality Associated with Influenza Pneumonia in Thailand: 2005-2008. *PLOS ONE*, **4**, e7776. https://doi.org/10.1371/journal.pone.0007776

[25] Katz, M.A., Tharmaphornpilas, P., Chantra, S., Dawell, S., Uyeki, T., Lindstram, S., *et al.* (2007) Who Gets Hospitalised for Influenza Pneumonia in Thailand? Implications for Vaccine Policy. *Vaccine*, **25**, 3827-3833. https://doi.org/10.1016/j.vaccine.2007.01.109

[26] Vonghrachnh, P., Simmernan, J.M., Phonekeo, D., Pansayavong, V., Sisouk, T., *et al.* (2010) An Early Report from Newly Established Laboratory-Based Influenza Surveillance in Lao PDR. *Influenza and Other Respiratory Viruses*, **4**, 47-52. https://doi.org/10.1111/j.1750-2659.2009.00120.x

[27] Suntarattwong, P., Sian-Nork, C., Chotip, Thongtipa, P. and Thawatsupha, P. (2007) Influenza-Associated Hospitalisation in Urban Thai Children. *Influenza and Other Respiratory Viruses*, **1**, 177-182. https://doi.org/10.1111/j.1750-2659.2007.00023.x

[28] Muyembe, T.J., Nkwembe, E., Bishamamba, S.K., Bankoshi, F., Ilunga, B.K., Katz, K.A., *et al.* (2012) Sentinel Surveillance for Influenza-Like Illness, Severe Acute Respiratory Illness, and Laboratory-Confirmed Influenza in Kinshasa, Democratic Republic of Congo, 2009-2011. *The Journal of Infectious Diseases*, **206**, S36-S40. https://doi.org/10.1093/infdis/jis537

[29] Radin, J.M., Katz, M.A., Tempia, S., Nzussouo Talla, N., Davis, R., Duque, J., *et al.* (2012) Influenza Surveillance in 15 Countries in Africa, 2006-2010. *The Journal of Infectious Diseases*, **206**, S14-S21. https://doi.org/10.1093/infdis/jis606

[30] Tamerius, J., Nelson, M., Zhou Steven, Z., Viboud, C., Miller, M. and Alonso, W. (2011) Global Influenza Seasonality: Reconciling Patterns across Temperate and Tropical Regions. *Environmental Health Perspectives*, **119**, 439-445. https://doi.org/10.1289/ehp.1002383

[31] Viboud, C., Alonzo, W.J. and Simonsen, L. (2006) Influenza in Tropical Regions. *PLOS Medicine*, **3**, e89. https://doi.org/10.1371/journal.pmed.0030089

[32] Heraud, J.M., Njouom, R., Rousset, D., Kadjo, H., Caro, V., Ndiaye, M., *et al.* (2012) Spatiotemporal Circulation of Influenza Viruses in 5 African Countries during 2008-2009: A Collaborative Study of the Institut Pasteur International Network. *The*

Journal of Infectious Diseases, **206**, S5-S13. https://doi.org/10.1093/infdis/jis541

[33] World Health Organization. Pandemic (H1N1) 2009-update 112. https://www.who.int/emergencies/disease-outbreak-news/item/2010_08_06-en

[34] Nzussouo, T., Michalove, J., Diop, O.M., Monteiro, M., Adje, H.K., Manoncourt, S., *et al.* (2012) Delayed 2009 Pandemic Influenza A Virus Subtype H1N1 Circulation in West Africa, May 2009-April 2010. *Infectious Diseases*, **206**, S101-S107. https://doi.org/10.1093/infdis/jis572