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Comparison of the Clinical Profile and Severity Factors of COVID-19 during the First 4 Waves in a Paediatric Population of Yaounde

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Abstract

Introduction: COVID-19 is an infectious disease that has been causing a global pandemic since 2019. Although clinical forms are generally less severe in children than in adults, children nevertheless present polymorphous clinical forms and severe cases that can lead to death. **Objective:** To describe the clinical presentations found in the different waves of COVID-19, and to highlight the different factors of severity. **Materials and Methods:** We conducted a cross-sectional study with retrospective and prospective data collection which lasted 7 months (from November 2021 to June 2022) and covered a study period from 6 March 2020 to 22 June 2022, *i.e.* 27 months. All patients aged 0 to 18 years, suspected of having COVID-19, confirmed by real-time RT-PCR or an antigenic Rapid Diagnostic Test or antibody were included. These patients were to be managed in the Mother and Child Centre of the Chantal Biya Foundation, as well as in the Specialised Centre for the Management of COVID patients, annex number II of the Yaoundé Central Hospital. The results were analysed using IBM SPSS.23 software. **Results:** We included 163 patients in our study. No paediatric patients were registered during the 3rd wave. The mean age of the patients in the study population was 13 ± 5 years with extremes from 15 days to 18 years. We had a female predominance with a sex ratio of 0.83. The most common comorbidity was asthma. The first wave presented mainly with respiratory symptoms such as dry cough and signs of respiratory distress. The second wave presented mainly with digestive symptoms such as diarrhoea, abdominal pain and vomiting. The fourth wave presented with ENT signs such as sore throat, and rhinorrhea. Factors associated with severity were mainly age less than five years (OR = 17.69), vomiting (OR = 6.50), presence of comorbidities (OR = 3.39), and

alteration of vital parameters such as bradypnoea (OR = 19.68), bradycardia (OR = 6.34), tachycardia (OR = 3.73), oxygen saturation < 95% (OR = 9.23). **Conclusion**: Clinical presentations varied between waves and the main risk factor was age under 5 years. The fourth wave was less severe than the second wave, which in turn was less severe than the first. ($4^{th} < 2^{nd} < 1^{st}$) which allows us to humbly recommend more screening for patients under 18 years of age with respiratory, ENT and digestive signs and special attention for those under 5 years of age.

Keywords

COVID-19, Children, Waves, Clinical Profile, Severity, Cameroon

1. Introduction

COVID-19 is an infectious disease caused by the SARS-CoV-2 virus. It is the cause of a global pandemic since 2019 and is a Public Health emergency [1]. In children, the clinical presentations are polymorphic, and less severe than in adults which means that clinicians do not think of it as a first-line condition, making it an under-diagnosed disease in the paediatric population in our context [2]. In some of these children, COVID-19 leads to severe disease and life-threatening complications. In addition to being under-diagnosed, the number of severe cases in Africa is higher than in the United States at 8% and at a rate of between 1% and 5% respectively [3].

In view of this, we set ourselves the objective of establishing the clinical profiles of each wave, comparing them and highlighting the severity factors of paediatric COVID-19 patients in two specialised management centres in Yaoundé.

2. Patients and Methods

We conducted a cross-sectional analytical study with retrospective and prospective data collection in the G Paediatrics Department and the intensive care unit of the Mother and Child Centre of the Chantal Biya Foundation, as well as in the COVID Specialised Patient Management Centre, annex number II of the Yaounde Central Hospital. The study lasted 7 months and the study period was from 6 March 2020 to 22 June 2022. We included patients aged 0 to 18 years considered as COVID cases according to the Scientific Council of Public Health Emergencies of Cameroon (by real time RT-PCR or Rapid Diagnostic Test antigen or antibody).

Criteria for inclusion of cases:

- Patients aged 0 to 18 years admitted for management of COVID-19 in the research facilities;
- Confirmed cases of COVID-19 according to the Scientific Council for Public Health Emergencies, *i.e.* antigenic test (COVID-19 RDT) or virological tests (RT-PCR);

- Informed consent from parents for prospective collections and assent from children over 12 years of age.

Disease severity criteria used were established by the Scientific Council of Public Health Emergencies of Cameroon:

For mild without comorbidity cases

- Asymptomatic or clinical signs:nasal congestion, sore throat and fever;
- Normal breathing;
- SpO_2 > 95% AA;
- No sign of gravity nor danger;
- Normal chest imaging.

For moderate cases

- Clinical signs: fever, asthenia, myalgia, diarrhea;
- No general sign of danger and/or gravity;
- SpO_2 > 95% AA;
- Cough or difficulty in breathing;
- Rapide respiratory rate;
- Imagery: 10 < damage ≤ 25%.

For severe cases

- Signs of respiratory distress;
- Signs of choc; severe dehydration;
- Liver damage, myocardial or coagulopathy;
- 92 ≤ SpO_2 < 95%; PaO_2/FiO_2 < 300 mmHg;
- Imagery: 25 < damage ≤ 75%.
- Presence of a comorbidity unbalanced

NB: the presence of one criteria is enough

For critical cases: severe form associated with

- Respiratory failure, requiring intubation;
- Signs of choc and/or organe failure (≥2);
- Chest Imaging: damage > 75%;
- PaO_2/FiO_2 < 200 mmHg;
- Lactates > 2 mmol/l.

NB: the presence of one criteria is enough

Sampling was consecutive, exhaustive and non-probabilistic during the study period. A complete clinical examination was performed on each included patient. Data entry was done using CS pro software and analysis using SPSS 23.0. Data were expressed as frequencies, means and percentages. An analysis of variance was used to assess differences between the study groups. An analysis of comparisons of the different waves was done with the Fischer exact test or the chi-square test. The significance level was set at 5%.

3. Results

We included 163 patients in our study, 29 patients in the first wave from March to December 2020, 124 patients in the second wave from December 2020 to July 2021, 0 patients in the third wave from August to November 2021, and 10 pa-

tients in the fourth wave from December 2021 to January 2022 (Figure 1 below represents the evolution of the pandemic in Cameroon with the different waves and numbers).

3.1. Socio-Demographic Characteristics

1) Age: the average age was 13 ± 5 years with the minimum and maximum age of (15 days) and 18 years respectively. The most represented age group was 15 - 18 years.

In the first wave, the median age was 14 years [6.5 - 17]. The minimum and maximum ages were 0.5 and 18 years. The most represented age group in the first wave was 15 - 18 years with 14 (48%) adolescents. In the second wave, the median age was 13 years [8.25 - 17]. The minimum and maximum ages were 0.04 and 18 years. The most represented age group was 15 - 18 years with 51 (41%) adolescents. We did not recruit inpatients in the third wave from August to November 2021. In the fourth wave, the average age was 7.3 ± 5.79 years. The minimum and maximum ages were 0.42 and 17 years. The most represented age group in the fourth wave was 0 - 4 years with 5 (50%) children.

2) The sex ratio in the general population was 1/1.20 (0.83). The sex ratio distribution in the waves was 1.07; 0.77 and 1 for the first, second and fourth waves respectively.

3.2. Clinical Characteristics According to the Waves

3.2.1. Comorbidities

In our study population, 12.3% of patients had at least one comorbidity. The most frequent comorbidity in the total population was asthma with 6 cases, *i.e.* about 3.7% of all patients and 30% of all comorbidities, followed by cardiac architecture abnormalities 3 cases (1.8%). One patient in the second wave had a history of smoking.

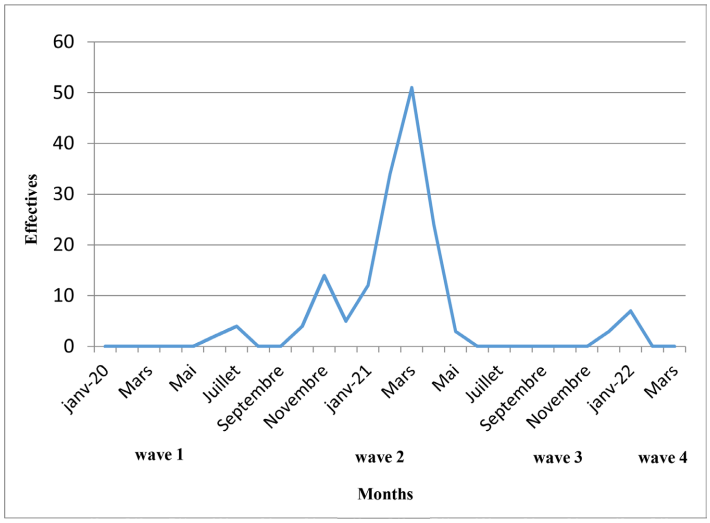

Figure 1. Evolution of the COVID-19 pandemic in the paediatric population of Yaoundé, with the representation of the different waves and the numbers in each wave.

See Table 1.

3.2.2. Clinical Symptoms on Admission

The clinical presentation of the first wave was mainly dominated by general and respiratory signs. The second wave was dominated by general and digestive signs. The fourth wave was dominated by general and ENT signs.

See Table 2.

Table 1. Distribution of comorbidities in different waves.

Variables	N (%) Wave 1	N (%) Wave 2	N (%) Wave 4
Sickle cell anemia	1 (3.4)	0 (0)	1 (10)
Asthma	0 (0)	6 (4.8)	0 (0)
Prematurity	0 (0)	2 (1.6)	0 (0)
Diabetis	0 (0)	1 (0.8)	0 (0)
Heart disease	1* (3.4)	1** (0.8)	1*** (10)
G6PD deficiency	1 (3.4)	1 (0.8)	0 (0)
HIV	1 (3.4)	0 (0)	1 (10)

*1 = Common arterial trunk; *1 = Subaortic membrane; ***1 = Pulmonary stenosis.

Table 2. Distribution of general signs and symptoms at patient admission

Variables	N (%) Wave 1	N (%) Wave 2	N (%) Wave 4
General signs			
Asthenia	11 (37.9)	72 (59.5)	3 (30)
Fever	3 (10.3)	17 (14)	3 (30)
Anorexia	0 (0)	3 (2.5)	2 (20)
Shivers	0 (0)	1 (0.8)	0 (0)
ENT symptoms	[9 (31%)]	[22 (18.3%)]	[5 (50%)]
Rhinorrhea	6 (20.7)	15 (12.4)	1 (10)
Snoring breath	0 (0)	0 (0)	2 (20)
Sore throat	2 (6.9)	4 (3.4)	2 (20)
Anosmia	3 (10.3)	3 (2.5)	0 (0)
Respiratory symptoms	[10 (34.4%)]	[25 (20.7)]	[3 (30%)]
Cough	7 (24.1)	21 (17.4)	2 (20)
Dyspnea	1 (3.4)	3 (2.5)	1 (10)
Chest pain	2 (6.9)	1 (0.8)	0 (0)
Ocular symptom			
Ocular pruritus	1 (3.4)	0 (0)	0 (0)
Digestifs symptoms	[13 (51.7)]	[136 (112.4)]	[25 (20.7)]

Continued

Diarrhea	6 (20.7)	61 (50.4)	3 (30)
Vomiting	0 (0)	10 (8.3)	2 (20)
Abdominal pain	7 (24.1)	65 (53.7)	0 (0)
Nervous symptoms			
Headache	0 (0)	3 (2.5)	0 (0)
Cutaneous symptoms			
Skin rash	1 (3.4)	3 (2.5)	1 (10)
Pruritus	0 (0)	0 (0)	0 (0)

3.2.3. Vital Parameters

Heart rate: Tachycardia was present in 9 (31%), 26 (22%) and 0% of patients in the first, second and fourth wave respectively.

Respiratory rate: Tachypnoea was present in 16 (55.2%), 42 (34.1%) and 1 (10%) patients in the first, second and fourth waves respectively.

Blood glucose: Hyperglycaemia was present in 2 (6.9) in the first wave and 2 (1.9) of patients in the second wave.

Temperature: Fever was present in 3 (10.3%), 7 (16.1%) and 2 (20%) patients in the first, second and fourth waves respectively.

Blood pressure: Hypertension was present in 2 (7.1%) in wave 1 and 9 (7.8%) of patients in wave 2.

Oxygen saturation: Hypoxaemia was present in 2 (6.8%), 3 (2.4%) and 1 (10%) patients in waves one, two and four respectively.

3.2.4. Physical Signs

The most common sign was mucocutaneous pallor with 60 (37%). It represented 4 (14%), 54 (70%) and 2 (20%) in the first, second and fourth waves respectively. Other signs were represented in the background, namely signs of respiratory distress, conjunctivitis and erythematous angina in the first, second and fourth waves respectively.

3.2.5. Clinical Stages (Figure 2)

The first and second waves were mainly moderate cases, 22 (76%) and 102 (82%) respectively. The fourth wave was mainly made up of asymptomatic and mild cases without comorbidities, 6 (60%).

Concerning the severe/critical stage, the first wave had 7 (24%), the second 22 (18%) and the fourth 3 (30%).

3.3. Severity Factors

3.3.1. Association between Socio-Demographic Parameters and Severity

The age groups significantly associated with severity were under 5 years and over 15 years. Those under 5 years of age were 17 times more likely to have severe forms (OR = 17.69) than the other age groups and those over 15 years of age

were about 5 times less likely to have severe forms (OR = 0.21). There was no significant association between gender and disease severity (*See* Table 3).

3.3.2. Association between Comorbidities and Severity

There was no statistically significant association between the presence of a particular comorbidity and the severity of the disease, however, the presence of comorbidities in general significantly increased the risk of developing a severe form of the disease by 3 times OR = 3.39 (1.18 - 9.76), while the absence of comorbidities reduced the risk of severity by 3 times OR = 0.30 (0.10 - 0.85).

3.3.3. Association between Symptoms on Admission and Disease Severity

Of all the symptoms, only vomiting was significantly associated with disease

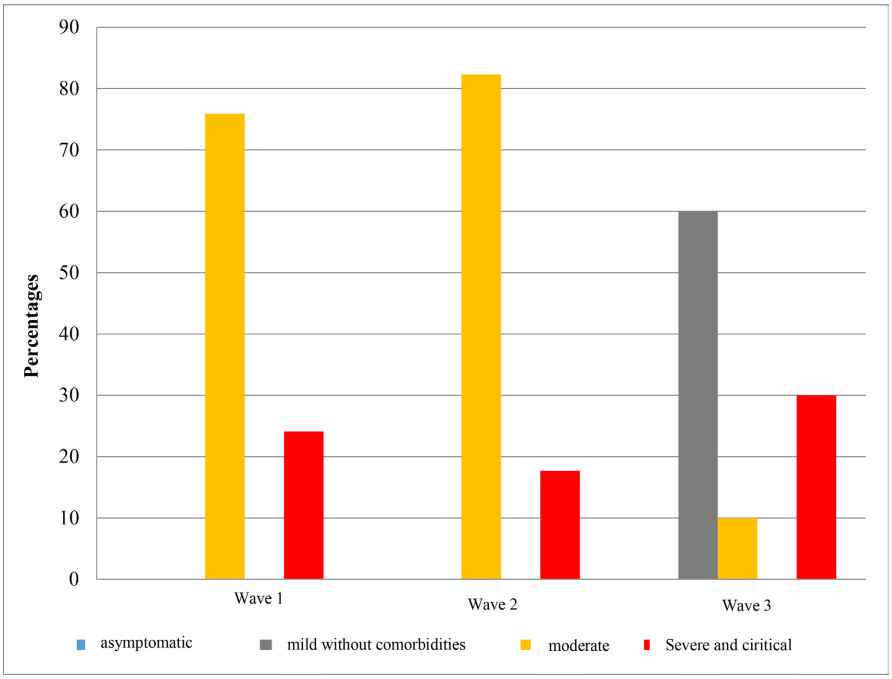

Figure 2. Distribution of Clinical Stages in the different waves.

Table 3. Socio-demographic parameters and severity in bivariate analysis.

Variables	Clinical stages		P value	OR (IC à 95%)
	Severe/Critical	other stages		
Age (Year)				
[0 - 5[	19 (65.5)	10 (34.5)	0.000	17.69 (6.8 - 45.99)
[5 - 10[	3 (11.5)	23 (88.5)	0.26	0.49 (0.14 - 1.73)
[10 - 15[	5 (11.9)	37 (88.1)	0.18	0.47 (0.17 - 1.31)
[15 - 20[	5 (7.6)	61 (92.4)	0.001	0.21 (0.08 - 0.59)
Sex				
Male	14 (18.9)	60 (81.1)	1.00	0.92 (0.42 - 2.00)
Female	18 (20.2)	71 (7.8)	0.83	1.09 (0.50 - 2.37)

severity, increasing the risk of having a severe form by 6.5 times; OR = 6.50 (1.91 - 22.14).

3.3.4. Association between Vital Parameters and Disease Severity

The vital parameters that increased the risk of having a severe form were; fever, increasing the risk of severity by 4.6 times (OR = 4.60), bradypnoea, increasing the risk by 19.7 times (OR = 19.68), bradycardia, increasing the risk by 6.3 times (OR = 6.34), tachycardia, increasing the risk by 3.7 times (OR = 3.73), and finally oxygen saturation < 95%, increasing the risk by 9.2 times (OR = 9.23).

In contrast, the parameters that acted as protective factors and reduced the risk of severity were: Normal heart rate, reducing the risk by 5.9 times (OR = 0.17) and oxygen saturation ≥ 95%, reducing the risk by 8.3 times (OR = 0.12).

We performed a multivariate analysis to eliminate confounding factors and found that age was a factor in severity, with an adjusted P-value of 0.000 and adjusted OR of 17.31.

3.4. Comparing the Different Waves in Clinical Terms

3.4.1. General Variables

Comparing the four waves epidemiologically, adolescents aged 15 - 18 were six times less likely to be affected in the fourth wave.

See Table 4.

3.4.2. Clinical Variables

When comparing the fourth wave with the first two on the clinical side, we observed that patients were 39 times more likely to have mild forms without comorbidities, but much less likely to have moderate forms (38 times less) (*See* Table 5).

4. Discussion

Our general objective was to describe the clinical presentations found in the different waves of COVID-19, to compare them and to highlight the different severity factors. The limitation of our study was that we had a selection bias in our

Table 4. Association between the different age groups and the fourth wave compared to the other waves.

Variables	N (%) Wave 4	N (%) Wave 1	N (%) Wave 2	P value (OR [IC 95%])
Age group (years)				
[0 – 0.99]	2 (25)	2 (25)	4 (50)	0.780 (6.13 [1.06 - 35.30])
[1 - 4]	3 (14.3)	2 (9.5)	16 (76.2)	0.090 (3.21 [0.76 - 13.56])
[5 - 9]	1 (3.8)	7 (26.9)	18 (69.2)	1.000 (0.57 [0.70 - 4.70])
[10 - 14]	3 (7.1)	4 (9.5)	35 (83.3)	0.720 (1.25 [0.31 - 5.08])
[15 - 18]	1 (1.5)	14 (21.2)	51 (73.3)	**0.049 (0.15 [0.02 - 1.22])**

Table 5. Associations between the most important clinical signs in our study and the fourth wave compared to the first two.

Variables	N (%) Wave 4	N (%) Wave 1	N (%) Wave 2	P value (OR [IC 95%])
Comorbidities				
Presence	3 (17.6)	3 (17.6)	11 (64.7)	0.072 (4.25 [0.99 - 18.32])
Absence	7 (4.8)	26 (17.8)	113 (77.4)	0.072 (0.24 [0.06 - 1.01])
Symptoms				
Asthenia	3 (3.5)	11 (12.8)	72 (83.7)	0.26 (0.97 [0.93 - 1.00])
Rhinorrhea	1 (4.5)	6 (27.3)	15 (68.2)	0.37 (3.07 [0.27 - 35.39])
Cough	2 (6.7)	7 (23.3)	21 (70)	0.10 (18.25 [1.36 - 245.19])
Abdominal pain	0 (0)	7 (9.7)	65 (90.3)	0.25 (1.04 [0.99 - 1.08])
Diarrhea	3 (43)	6 (8.6)	61 (87.1)	0.09 (0.96 [0.91 - 1.00])
Physical signs				
Skin rash	1 (20)	1 (20)	3 (60)	0.10 (18.25 [1.35 - 245.18])
Tachycardia	0 (0)	9 (25.7)	26 (74.3)	1.00 (1.02 [0.99 - 1.04])
Tachypnea	1 (1.7)	16 (27.1)	42 (71.2)	0.39 (0.99 [0.95 - 1.01])
High blood pressure	0 (0)	2 (12.8)	9 (81.8)	1.00 (1.01 [0.99 - 1.02])
Low oxygen saturation	1 (16.7)	2 (33.3)	3 (50)	0.04 (0.83 [0.59 - 1.18])
Clinical stages				
Severe/Critical	3 (9.4)	7 (21.9)	22 (68.8)	0.14 1.83 (0.45 - 7.52)
Moderate	1 (0.8)	22 (17.6)	102 (81.6)	0.00 (0.026 [0.00 - 0.21])
Asymptomatic and mild	6 (100)	0 (0)	0 (0)	0.00 (39.25 [14.92 - 103.27])

study, due to the fact that the recruitment of our patients was done in intensive care units and in specialised centres that did not receive asymptomatic cases. Despite this limitation, the strength of our study was that we conducted a study in specialised paediatric COVID-19 referral centres in the city of Yaoundé with specialists in the disease, which guarantees the reliability of our clinical examinations, in addition, we had patients from all regions of Cameroon, which makes our study generalisable in the national territory.

The mean age of the study population was 13 ± 5 years with extremes of 0.04 years (15 days) and 18 years. In the whole population, the most represented age group was 15 - 18 years (66%). These results are similar to those of Meguieze *et al.* [2] who calculated the prevalence of COVID-19 in the city of Yaoundé. With an age range of 0 - 19 years, it had a mean age of 10.89 ± 7 years. This result was different from that of Camara *et al.* [4] who evaluated the epidemiological and clinical profile of children with COVID in a town in Guinea. It had a more predominant age range of 0 - 4 years and an average age of 7 years. This difference could be due to the age of inclusion of the patients. Camara limited himself to 16

years, which also lowered his average age, whereas we included patients up to the age of 18.

The female sex was the most represented in our study with 89 (54.6%) girls and 74 (45.4%) boys. The sex ratio was 0.83. This is similar to the study by Camara *et al.* [4] who found a female predominance of 60.32%, this predominance in Camara was due to the demography of Guinea, which is predominantly female. But a study by Meguieze *et al.* in the vicinity of Yaoundé [2] showed a male predominance of 52%. This is probably due to the male predominance of the Cameroonian population under 20 years of age. In our study, we did not find an explanation for the female predominance and we think it is probably due to chance.

In our study population, 12.3% of patients had at least one comorbidity. The most frequent comorbidity was asthma. This result is similar to that of Adeel butt *et al.* [5] who compared the Omicron variant with the Delta variant in Qatar. She found that 14% of the patients had at least one comorbidity and 98% of them had chronic lung disease, especially asthma. This could be explained by the fact that corona virus disease has variants that have a tropism for the respiratory system, with ACE 2 receptors on it. This respiratory tropism means that patients with chronic respiratory comorbidities have less immune protection, and are therefore more likely to be infected than others without comorbidities [6].

Regarding clinical signs, the first wave was mainly dominated by general signs (asthenia 11 (37%) and fever 3 (10.3%)), respiratory (cough 7 (24.1%) and dyspnoea 1 (3.4%)). This result is similar to that of Patel *et al.* [7] who performed a meta-analysis of the clinical presentation of paediatric patients in the first wave. They found that 48% had a cough and 47% had a fever. This could be explained by the high tropism of the original variant for the respiratory system giving severe viral pneumonia.

The clinical presentation of the second wave was dominated by general signs (asthenia 72 (59.5%) and fever 17 (14%)), digestive signs (diarrhoea 61 (50.4) and abdominal pain 65 (53.7)). This result differs from that of Meyer *et al.* [8] who found a predominance of general signs with fever 25%, followed by cough (23%) and rhinorrhea (23.7). Gastrointestinal symptoms in this study came with a proportion of 6.8%. This discrepancy could be explained by the fact that some populations may have a higher expression of ACE2 receptors in the gastrointestinal tract compared to others. [9] Finally, we can speculate that these symptoms may be associated with a complication of COVID-19 called Multi-systemic Inflammatory Syndrome of Children (MIS-C), which combines fever, biological inflammatory syndromes, D-dimer elevation and involvement of at least two systems. [10]

The fourth wave was dominated by general signs (asthenia 3 (30%), fever 3 (30%)) followed by ENT signs (rhinorrhea 1 (10%), sore throat 3 (30%)) and finally respiratory symptoms such as cough 2 (20%) and dyspnea 1 (10%). This result is similar to that of Jeané *et al.* [11] who found a predominance of general signs such as fever at 46%, followed by cough at 40% and dyspnoea at 22%. This

could be explained by the fact that the fourth wave Omicron variant also has a high tropism for the airways, but more precisely the upper airways [11].

Age less than 5 years as the main severity factor is a similar result to that of Adeel Butt *et al.* [5] who did a comparative study in Qatar in children comparing the waves. They found that children under 6 years of age had a higher risk of severe forms than other age groups. This could be explained by the weak immune response of this age group compared to others who have already developed an immune response to other circulating influenza viruses. Also, the anatomy of the respiratory tree in children under five years of age is more susceptible to this type of infection.

The risk of severity when saturation was below 95% was nine times higher than in those with normal saturation. This result is similar to that of Abdelbassat *et al.* [12] who found an association between the severity of the infection and desaturation on the one hand and between mortality and hypoxia on the other. This could be explained by the fact that in severe forms of the infection, the virus causes a severe viral pneumonia which disturbs haematosis and reduces oxygen saturation.

We found a risk of developing a severe form when vomiting. This result is similar to that of Graff *et al.* [13] who found vomiting to be a predictive factor for severity in a cohort of 454 children in the USA. This could be explained by the fact that vomiting would potentiate dehydration which would increase the risk of mortality.

In our study, one was three times more likely to have a severe form if one had a pre-existing comorbidity than if one did not. This result is similar to that of Funk *et al.* [14]. He looked at factors of severity in children in Canada and the USA and found a twofold increased risk of severity in children with a comorbidity. The explanation is that comorbidities such as asthma and heart disease are organ disorders that are themselves target organs for SARS-CoV-2. Thus, COVID-19 infection in asthmatics would increase the risk of severe attacks, and asthma would aggravate the respiratory distress caused by COVID-19. Cardiac architectural abnormalities would complicate any cardiac damage caused by SARS-CoV-2.

Fever, bradypnoea, bradycardia and tachycardia are already included in the WHO and Cameroon criteria [15] for classifying patients as severe.

5. Conclusion

The most represented age group was 15 - 18 years, and the most common signs were respiratory, digestive and ENT. General signs such as asthenia and fever were present in all waves. In the first wave, patients presented mainly with respiratory signs and this was the most severe wave.

The second wave was more moderate and patients presented with digestive signs. The fourth wave was the mildest and patients presented mainly with Otho-Rino-laryngology signs. Factors associated with severity were mainly age

below five years, oxygen desaturation, vomiting, presence of comorbidities and alteration of vital parameters namely fever, bradypnoea, bradycardia and tachycardia.

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Conflicts of Interest

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

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