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Vaccination and Measles Epidemic in the Republic of Congo

Léa Gwladys Gangoue[1,2], Yanne Mavougou[1,2], Fabien Rock Niama[1,2], Pembe Issamou Mayengue[1,2], Etienne Nguimbi[2]

[1]National Public Health Laboratory (LNSP), Ministry of Health and Population, Brazzaville, Republic of Congo
[2]Cellular and Molecular Biology Laboratory (BCM), Faculty of Sciences and Techniques, Marien Ngouabi University, Brazzaville, Republic of Congo
Email: leagangoue3@gmail.com

Abstract

Measles is a highly infectious, vaccine-preventable viral disease. Often forgotten, it is potentially fatal. Its main symptoms are: fever, cough, conjunctivitis, rhinitis and skin rash. Serological diagnoses by ELISA test based on the detection of anti-measles virus immunoglobulins M and G (IgM and IgG), are used respectively for the confirmation of suspected cases notified by means of clinical signs of the disease in health structures of the twelve departments of the Republic of Congo involved in the epidemiological surveillance of the disease, and for the evaluation of the immunity conferred by vaccination. During 2021, 459 suspected cases of measles were reported and sampled throughout the country, despite the administration under the Expanded Routine Immunization Program (EPI), of 2 doses of the combined measles-rubella vaccine (RR1 and RR2) in 2020. The notification rate was higher in the south of the country, more precisely in the health structures of the departments of Pointe-Noire (42%) and Brazzaville (11%). During the year 2021, 459 suspected cases of measles were notified and sampled throughout the country with a high notification rate in the south of the country, more precisely in the health structures of the Pointe-Noire departments (42%) and Brazzaville (11%). The samples consisting of human blood (serum) were sent to the National Public Health Laboratory and analyzed by various ELISA tests for the detection of anti-measles immunoglobulins M and G. The analysis of the results obtained shows that the measles virus circulated in all departments of the country. 154 cases (33.55%) were confirmed positive by IgM ELISA and 98 positive cases (63.63%) were patients vaccinated against measles. Vaccination coverage in RR1 of [50% - 95% [(first dose) as well as the lowest RR2 < 50% (second dose) undoubtedly because the COVID-19 pandemic could be the cause of the high frequency of cases positive vaccinated. The non-detection of IgG immunoglobulins in vaccinated patients observed by IgG ELISA tests revealed that 63.26% of vaccinated patients were

not immunized against the measles virus. These results confirm those obtained during the Elisa IgM analysis and make it possible to deduce that the quality, the number of doses not properly administered, the individual characteristics of the people as well as the poor conservation of the administered vaccine (non-compliance with the cold chain) would explain the high proportion of positive cases of vaccinated measles observed.

Keywords
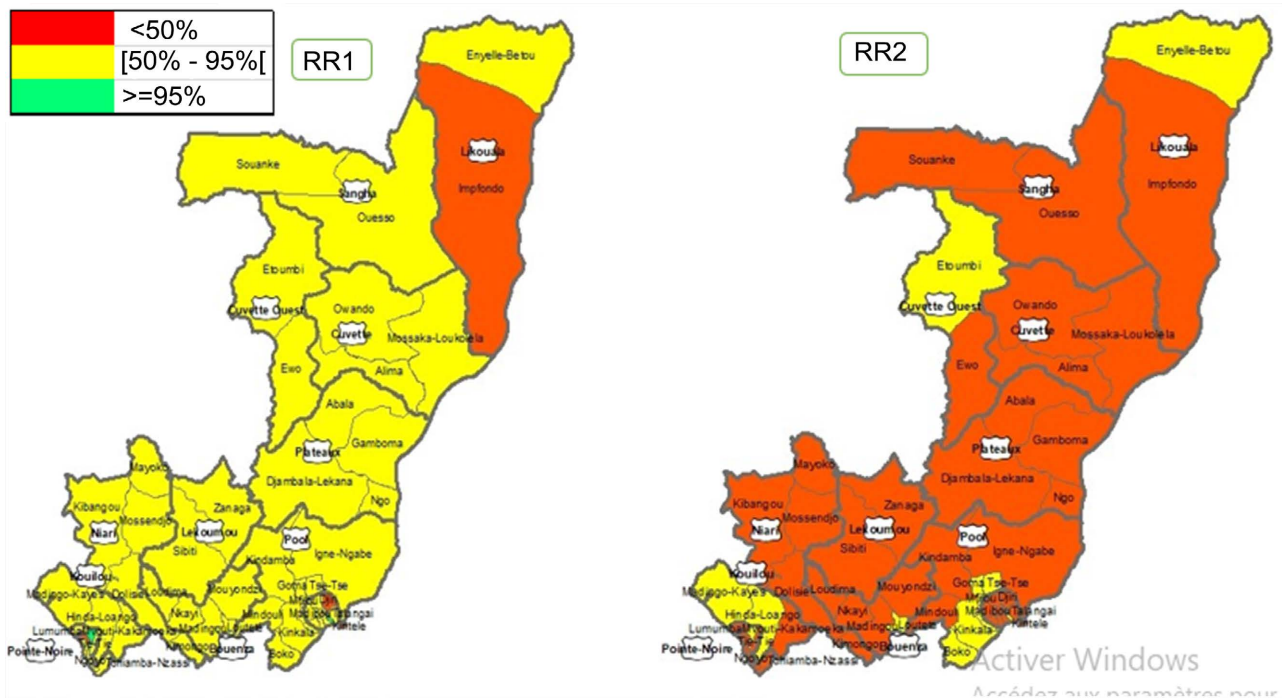
Vaccination , Measles Epidemic

1. Introduction

Measles is a highly contagious viral disease with a reproduction rate of between 12 and 18 in an at-risk population [1]. It is transmitted through the air or by direct contact with the secretions of an infected person [2]. Multiple clinical signs have been reported and the most serious forms of the disease result in high fever (39˚C - 40˚C), pneumonia, diarrhea, dehydration, vomiting and encephalitis. This infection can lead to death, especially in children aged 0 to 5 years (2 - 4). Indeed, in order to eliminate measles, the WHO recommends that countries achieve a minimum vaccination coverage of 95%, with equitable administration of different doses of vaccine in the hope of achieving herd immunity and stopping the circulation of the virus [3] [4].

Despite significant efforts by the international community, it remains a major public health problem, both in countries with limited resources and in developed countries despite the integration of vaccines into the expanded vaccination program in all countries of the world [5].

In the Republic of Congo, an epidemiological surveillance system for measles has been in place since 2005 involving the health structures of the twelve departments of the country (Pointe Noire, Kouilou, Niari, Bouenza, Likouala, Sangha, Lekoumou, Plateaux, Pool, the Central Cuvette, the West Cuvette and Brazzaville). Sporadic cases were reported and confirmed in the south of the country in 2007 and gradually in the center and then the north of the country [6]. In recent years, the number of positive cases recorded is considerable and epidemics have been declared in our country by the Ministry of Health and Population, despite vaccination campaigns against measles organized throughout the Republic of the Congo. During 2021, suspected cases of measles were reported and confirmed despite the administration, as part of the Expanded Routine Vaccination Program (EPI), of 2 doses of the combined Measles-Rubella vaccine (RR1 and RR2) introduced in 2019 (Figure 1). This work aims to determine the causes of confirmed positive cases of measles in the Republic of Congo in 2021 after the two routine vaccinations in RR1 and RR2 of 2020, more precisely, to describe the distribution of confirmed cases of measles according to vaccination status in during the year 2021 based on the analysis of the results of serological tests (ELISA IgM and IgG) carried out at

Figure 1. Vaccination coverage in RR1 and RR2 2020.

the National Public Health Laboratory. Measles surveillance today obeys a code which authorizes the confirmation of cases by simple epidemiological link, especially during periods of epidemic; this work is part of the aim of determining the causes of positive cases of measles in the Republic of Congo in 2021 after the two vaccination coverage in RR1 and RR2 of 2020, more specifically, to describe the distribution of confirmed cases of measles according to the vaccination status during the year 2021 based on the analysis of the results of serological tests (ELISA IgM and IgG) carried out at the National Public Health Laboratory.

2. Material and Methods

2.1. Material

The biological material consisted of samples of human blood (serum) taken from vaccinated or unvaccinated children suspected of having measles, whose clinical signs suggestive of measles were highlighted by health workers, in the health structures involved in measles surveillance.

2.2. Methods

This is a descriptive study of all suspected cases of measles notified in the different health structures of all departments of the country, during the period January 1 to December 31, 2021. A suspected case of measles was defined as any person presenting a widespread maculopapular rash and fever, and any of the following symptoms: cough, coryza (runny nose), or conjunctivitis (red eyes). While the laboratory-confirmed case is a suspected case whose laboratory results indicate infection by the detection of measles IgM.

A case notification form was used to obtain sociodemographic information (department, age, sex, vaccination status) and clinical information (date of appearance of signs after suspicion).

In each department, a focal point has been designated, located at the prefecture of this department and attached to the vaccination program in contact with the agents of the health structures of the department. Once a clinical description corresponds to the disease, health workers are responsible for collecting the samples. The informed focal point is responsible for shipping the samples. 5 mL of whole blood was collected by venipuncture into the dry tube. Identified (data on the passion and the date of collection, Centrifuged at 1000 revolutions for 10 min in order to separate the serum. The sera were stored for a maximum of 7 days between 4 and 8°C, beyond that at −20°C. Samples were transferred within 24 to 72 hours in an insulated cooler maintained at 2°C - 4°C to the WHO country office where the samples were registered (assignment of the epidemiological number and transferred to the National Public Health Laboratory for analysis.

The samples from suspected measles cases were analyzed using the EUROIMMUN IgM kit (following the manufacturer's instructions) for the detection of type M immunoglobulins using the ELISA (Enzyme-Linked Immunosorbent Assay) ELISA Anti-Measles Virus technique. All samples from confirmed positive or ELISA IgM-positive vaccinated cases were then analyzed always using the ELISA technique for the detection of immunoglobulins type G with the EUROIMMUN IgG kit [7].

- **IgM ELISA method**

The samples to be analyzed (serum) were previously treated with RF-Absorbent which binds to the anti-Measles virus IgG and thus eliminates the virus-specific IgG; the anti-measles virus IgM antibodies present in the sample to be tested bind to the antigen fixed in the reaction wells of the test plate. The anti-IgM POD Conjugate then binds to these specific antibodies, the enzymatic part of the conjugate transforms the chromogen solution by coloring it blue. This reaction is then stopped by the addition of the POD stopping solution which colors the solution yellow. IgM directed against cellular antigens is revealed in the same way in wells coated with control antigens. The difference in coloring intensity obtained for the patient's sample between the well containing the control antigen makes it possible to measure the quantity and the immunochemical reaction of the antibody directed against the virus sought.

- **IgG ELISA method**

The anti-measles virus IgG antibodies present in the sample to be tested bind to the antigen fixed in the reaction wells of the test plate. The anti-IgG POD Conjugate then binds to these specific antibodies, and the enzymatic part of the conjugate transforms the chromogen solution by coloring it blue. This reaction is then stopped by the addition of the POD stopping solution which colors the solution yellow. IgG directed against cellular antigens is revealed in the same way in wells coated with control antigens. The difference in coloring intensity ob-

tained for the patient's sample between the well containing the control antigen makes it possible to measure the quantity and the immunochemical reaction of the antibody directed against the virus sought.

The controls included in the reagent kits were used as well as controls made from control pools or serum mixtures to ensure the quality of the tests performed.

The test validation algorithm was as follows: the OD (optical density) of the calibrator must be greater than 0.140; a sample was negative if the OD Sample/DO Calibrator ratio was less than 0.80; a sample was positive if the OD Sample/DO Calibrator ratio was greater than 1.10; a sample was undetermined if the Sample OD/Calibrator OD ratio was between 0.80 and 1.10. In the latter case, the test must be repeated.

2.3. Results Analysis

The statistical analysis was carried out using SPSS.22 software. Microsoft Excel was used to develop graphs of epidemiological data.

3. Results
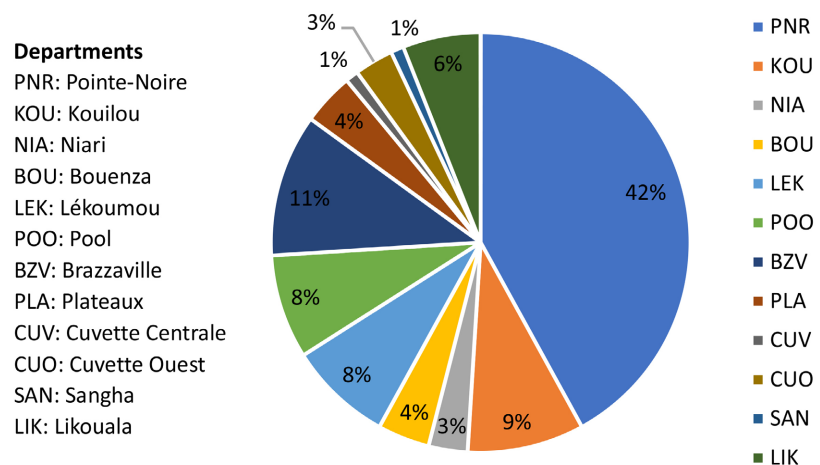
3.1. Notification of Suspected Measles Cases

- Distribution of suspected cases of measles notified by department

A total of 459 (2021) suspected cases of measles were reported in all departments with high reporting (42%) in Pointe-Noire and very low reporting in Sangha, Cuvette Est and Cuvette Ouest (1%) (**Figure 2**).
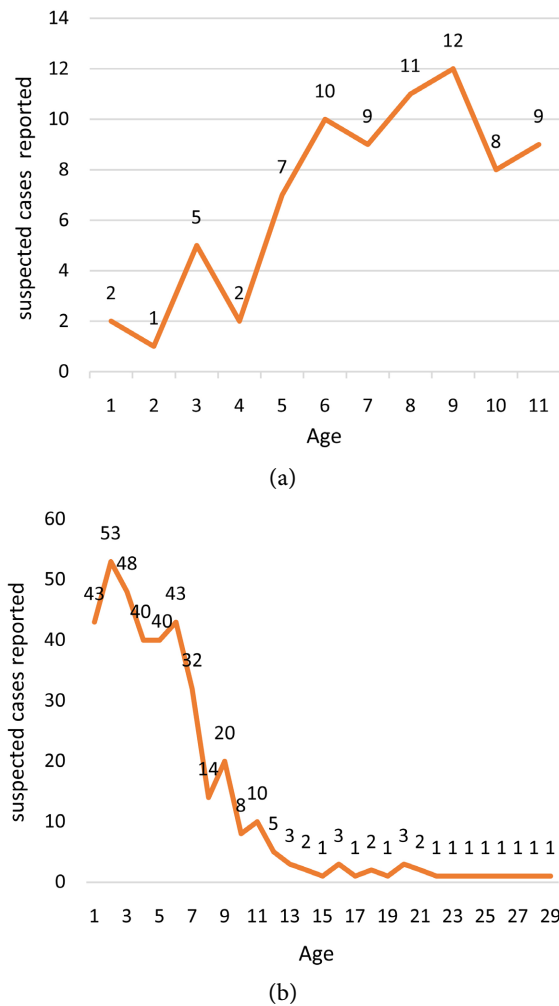
- Distribution of suspected measles cases notified by age

76 suspected cases (16.57%) were reported in children under one year old, and the most represented in the population were those over 5 months old (**Figure 3(a)**).

383 suspected cases were reported in patients aged 1 year to older and the number of suspected cases varies depending on the year and decreases as the age of the patients increases (**Figure 3(b)**).

Figure 2. Distribution of suspected measles cases notified by department. *P*-value = 0.010 > 0.005.

(a)

(b)

Figure 3. (a): Distribution of suspected measles cases notified by age (months). *P*-value = 0.009 > 0.005; (b): Distribution of suspected measles cases notified by age (years). *P*-value = 0.012 > 0.005.

- **Distribution of suspected measles cases notified by sex**

We recorded 233 (50.76%) male patients and 226 (49.23%) female patients. The number of cases reported was approximately the same among boys and girls (Figure 4).
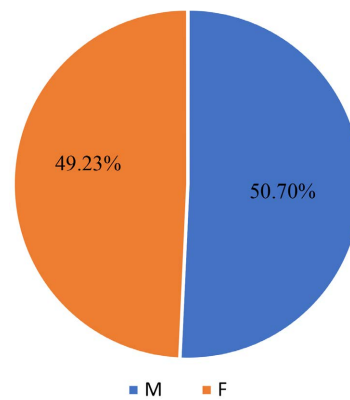
- **Distribution of suspected measles cases reported according to vaccination status**

350 (76.25%) suspected cases were reported in unvaccinated patients and 109 (23.74%) in vaccinated patients (Figure 5).
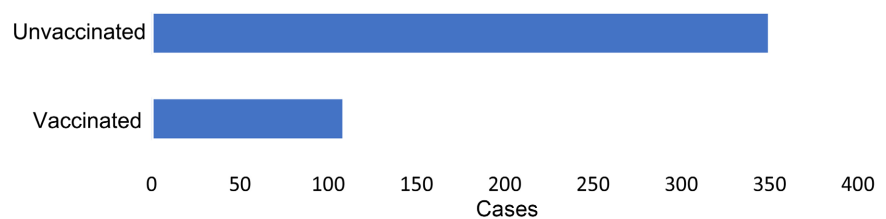
3.2. Suspected Cases of Measles Confirmed in the Laboratory

Figure 6 shows the results of IgM Elisa analyzes of reported suspected measles cases.
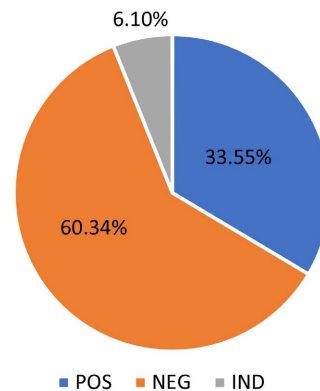
154 (33.55%) suspected cases were confirmed positive for measles, while 277 (60.34%) and 28 (6.1%) gave respectively negative and undetermined results after analysis.

Figure 4. Distribution of suspected measles cases notified by sex. *P*-value = 0.01 > 0.005.

Figure 5. Distribution of suspected measles cases notified according to vaccination status. *P*-value = 0.008 > 0.005.

Figure 6. Distribution of confirmed suspected measles cases.

- **Distribution of confirmed suspected cases of measles by department**

Suspected cases of measles have been confirmed in all departments, especially in the southern part of the country. The highest incidence was observed among children notified in the Pointe Noire department with a frequency of 44.15% (68 positive cases) (**Figure 7**).

- **Distribution of confirmed suspected measles cases by age**

22 (14.28%) suspected cases were confirmed positive in children less than 1 year old, the highest incidence was observed in children 5 - 10 months old (**Figure 8(a)**). 132 suspected cases were confirmed positive in children aged one year and older, with rates 79.87% (123 cases) in children aged 1 - 15 years and 9 cases (5.84%) aged 16 years and older (**Figure 8(b)**).
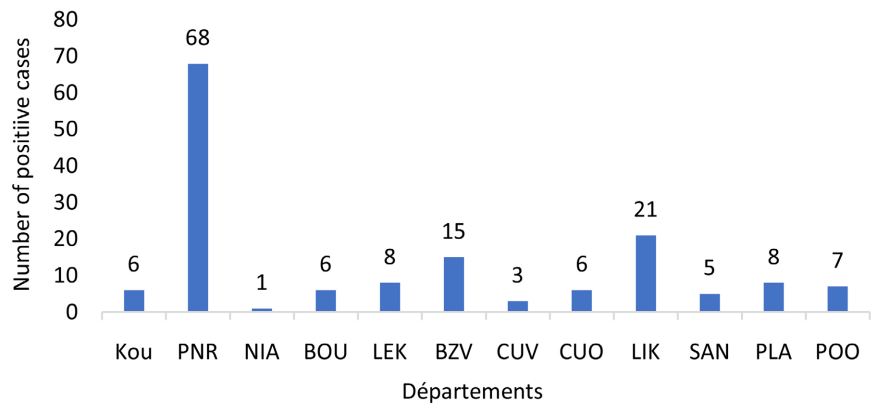
Figure 7. Distribution of suspected measles cases by department.
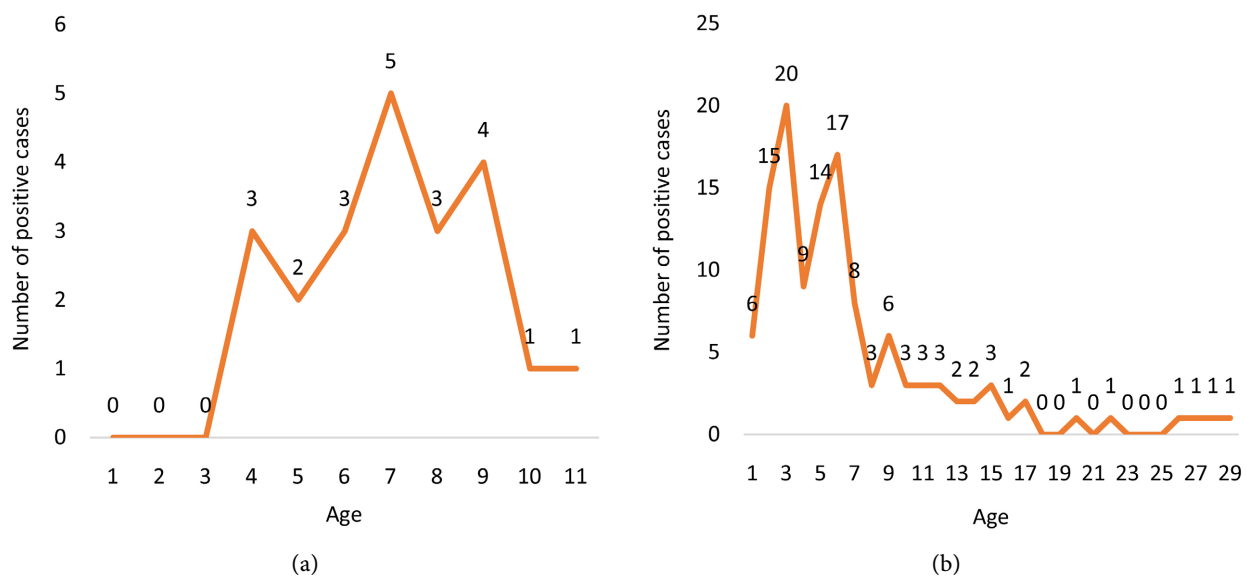

(a)

(b)

Figure 8. (a): Distribution of positive measles cases reported by age (months), *P*-value = 0.016 > 0.005; (b): Distribution of positive measles cases reported by age (years), *P*-value = 0.011 > 0.005.

- **Distribution of confirmed suspected measles cases by sex**

  Suspected cases of measles were confirmed in male and female patients. Women were slightly more exposed to the disease than men with frequencies of 54.54% and 46.10% respectively (**Figure 9**).

- **Distribution of suspected cases of measles confirmed positive according to vaccination status**

  Analysis of the results show that suspected cases of measles were confirmed positive in vaccinated patients as well as those not vaccinated against the measles virus. 98 vaccinated positive cases (63.63%) and 56 unvaccinated positive cases (36.36%) were recorded (**Figure 10**).

### 3.3. Detection of Immunoglobulin G (IgG) in Vaccinated Measles Positive Cases

Analysis of the results of 98 vaccinated positive cases by IgG ELISA shows that

IgG immunoglobulins were detected in 31 (31.63%) of vaccinated positive patients, not detected in 62 (63.26%) of vaccinated patients, while in 5 (5.10%) patients detection was undetermined 63.26% of vaccinated patients were not immunized against the measles virus (Figure 11).
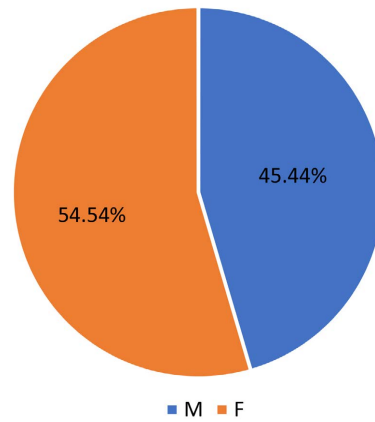
Figure 9. Distribution of confirmed suspected measles cases by sex. *P*-value = 0.009 > 0.005.
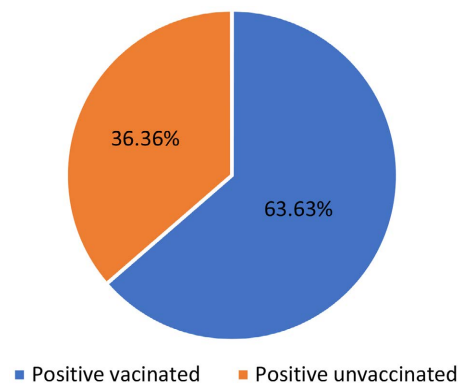
Figure 10. Distribution of suspected confirmed measles cases according to vaccination status.
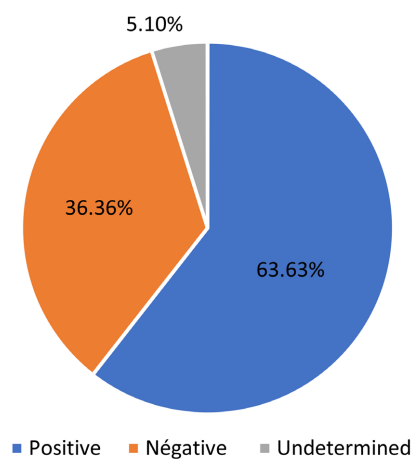
Figure 11. IgG level detected in vaccinated positive cases.

4. Discussion

This study was a means of describing the distribution of confirmed cases of measles according to vaccination status during the year 2021 based on the analysis of the results of serological tests (ELISA IgM and IgG). The high notification of suspected cases as well as the positive confirmation observed in the southern part of the country with 42% of notified cases, and 44.15% of positive cases in Pointe observed could be explained respectively by the concentration of the population in this part of the country, favoring the circulation of the measles virus and high attendance of health areas by the population. The observed high frequency of suspected cases of measles confirmed for females does not allow the gender factor to be implicated as a risk factor for measles virus infection because it depends on the patients presenting in the different health districts and this is proven by the P-value $= 0.01 > 0.05$. The frequencies of confirmed positive cases in different age groups, 79.87% in children aged 1 - 15 years and the highest incidence observed in children aged 5 - 10 months are close to those observed in the annual data of measles in France [8]. These results can be explained by taking the first dose of the measles vaccine only from 9 months and a second dose at 18 months according to the country's vaccination schedule.

The frequencies of confirmed positive cases according to vaccination status obtained showed that 63.46% of vaccinated patients were exposed to the virus. These results are close to those obtained during a study on the epidemiological surveillance of measles in Brazzaville [9] showing a distribution of confirmed positive measles cases high among vaccinated patient at 65.67% in the study population. The low vaccination coverage during the second round of vaccination (RR2) less than 50% which could be due to the COVID-19 pandemic (Figure 1) would be one of the factors of exposure of patients to the virus although having received the first RR1 dose (vaccination coverage: [50% - 95%[) because a single dose of RR vaccine cannot confer complete immunity against the measles virus, and 5% - 10% of people vaccinated against measles do not respond at the 1st dose [10]. Furthermore, the high frequency (63.91%) of non-detection of IgG in vaccinated patients confirms that the majority of patients have not been immunized against the measles virus and also leads to deduce that the quality, number of male doses administered and the individual characteristics of the vaccinated people [10] as well as the poor conservation of the administered vaccine, that is to say the non-compliance with the cold chain, could explain the results the high proportion of cases measles positive vaccinated.

5. Conclusion

The study made it possible to determine the prevalence and evaluate the distribution of confirmed cases of measles according to vaccination status during the year 2021 after vaccination coverage in RR1 and RR2 of 2020. Suspected cases were notified and confirmed across the entire country among vaccinated and unvaccinated patients showing that the measles virus has circulated in all depart-

ments of the Republic of Congo with a high incidence of positive cases in the southern part of the country. The age range of patients infected with the measles virus in 2021 in the Republic of Congo is 1 - 15 years old. From the point of view of vaccination status, a high frequency of vaccinated positive cases (63.46%) was observed. The vaccination coverage in RR1 of [50% - 95% [(first dose) as well as the lowest in RR2 < 50% (second dose) undoubtedly because the COVID-19 pandemic could explain the results observed. The non-detection of IgG immunoglobulins in vaccinated patients observed by IgG ELISA tests revealed that 63.26% of vaccinated patients were not immunized against the measles virus. These results confirm those obtained during the Elisa IgM analysis and allow us to deduce that the quality, the number of doses not properly administered, the individual characteristics of the people as well as the poor conservation of the administered vaccine (non-compliance with the cold chain) would explain the high proportion of positive measles cases vaccinated.

Conflicts of Interest

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

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