



Reduction of Laboratory-Confirmed Rubella Cases after introduction of Measle-Rubella (MR) vaccine in Côte d'Ivoire

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ABSTRACT

Rubella is generally a mild viral infection, but it poses a major public health problem due to its teratogenic effects, which can lead to congenital rubella syndrome (CRS). In Côte d'Ivoire, the measles and rubella (MR) vaccine was introduced into the Expanded Program on Immunization in 2018. A retrospective analysis of laboratory-confirmed rubella cases was conducted using data from the integrated measles and rubella surveillance system between January 2013 and December 2024. Serum samples from suspected measles cases were tested for the presence of rubella-specific IgM antibodies by ELISA. Positivity rates were analyzed by age group, period, and geographic distribution, and trends before and after the introduction of the MR vaccine were compared. Of the 25,244 samples tested, 1,463 (5.8%) were positive for anti-rubella IgM. Positivity rates were highest before 2018 and decreased significantly after the introduction of the MR vaccine, from 17.2% to 3.2% ($p < 0.001$). Higher positivity was observed in school-aged children and adolescents, with heterogeneous geographic distribution and a seasonal peak between February and May. Rubella circulation in Côte d'Ivoire has decreased significantly since the introduction of the MR vaccine. However, the persistence of transmission in certain age groups highlights the need to strengthen surveillance and implement targeted catch-up vaccination strategies to prevent CRS and eliminate rubella.

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Introduction

Rubella is a viral respiratory infection that occurs worldwide and manifests as a mild, rash-associated fever, primarily in children. Rubella is caused by a virus of the matonaviridae family (ICTV, 2024; Walker et al., 2019). It is an RNA virus with a single serotype, and humans are its only known host. Its public health impact is mainly due to the teratogenic potential of the virus, particularly when infection occurs early in pregnancy, leading to what is known as Congenital Rubella Syndrome (CRS) (Winter et Moss, 2022). In 1993, the International Task Force for Disease Eradication released its recommendations identifying which diseases were considered potentially eradicable at the time. Rubella was included among the diseases deemed capable of being eradicated (ITFDE, 1993). Despite the availability of the rubella vaccine since 1969 (Reef & Plotkin, 2006), many African countries were slow to introduce it into their Expanded Program on Immunization (EPI). This delay may be explained by several factors: the initial priority given to measles control a more visible disease associated with higher child mortality, financial and logistical challenges related to implementing the combined measles-rubella (MR) or measles-mumps-rubella (MMR) vaccine, the need for reliable epidemiological data to justify vaccine introduction, and the WHO requirement to achieve at least 80% coverage of the first measles dose before adding the rubella component to the combined vaccine (WHO, 2020).

In Côte d'Ivoire, the combined live attenuated measles and rubella (MR) vaccine was introduced into the EPI in 2018, targeting children aged between 9 and 11 months with catch-up campaigns (SIA) conducted in 2022 targeting unimmunized populations immunized populations aged 9 months to 5 years (single dose) and those aged 6 to 14 years (single dose regardless of their vaccination history). No systematic booster was deployed, in accordance with the WHO protocol recommending a single dose for lasting immunity against rubella (efficacy >95% after complete vaccination). This measure aimed to broaden vaccine protection by including the ru-

bella component, thereby reducing the vulnerability of young children and ultimately women of childbearing age to the risk of CRS. However, the success of this strategy depends on actual vaccination coverage, case surveillance, and the system's capacity to detect asymptomatic infections and mild cases. In this context, there remain areas in Côte d'Ivoire where rubella continues to circulate, often silently, with potentially susceptible populations for whom the MR vaccine may not yet provide sufficient protection. Although surveillance data from the integrated measles and rubella system are collected, they remain insufficiently analyzed, limiting an accurate assessment of the epidemiological situation. The objective of this study is to describe the epidemiological profile of confirmed rubella cases in Côte d'Ivoire from 2013 to 2024 using data from the integrated measles and rubella surveillance system, in order to provide useful information to guide prevention interventions.

Materials and Methods

Study Setting

The study was conducted using data from the national measles surveillance system. This surveillance is coordinated by the Directorate for the Coordination of the Expanded Program on Immunization (DCPEV), a priority program of the Ministry of Health and Universal Health Coverage aimed at protecting early childhood. The surveillance system relies on a reporting network for suspected measles cases across all health districts in the country. The Institut Pasteur of Côte d'Ivoire (IPCI) is part of this system as the reference laboratory responsible for case confirmation. The data used for this study cover the period from January 2013 to December 2024. These data include sociodemographic and clinical information on recorded suspected cases.

In addition, the laboratory regularly participates in external quality assessment (EQA) programs organized by the World Health Organization (WHO) and the Centers for Disease Control and Prevention (CDC, Atlanta, USA), to ensure compliance with analytical performance standards. Strict adherence to standard operating procedures (SOPs) and full traceability of samples and reagents also contributed to reinforcing the quality of the generated data.

Expanded Program on Immunization (EPI) and Measles-Rubella

The Expanded Program on Immunization (EPI) is the national framework for all immunization activities in Côte d'Ivoire. Launched in 1978, it aims to protect populations against several vaccine-preventable diseases.

The EPI is implemented on an ongoing basis by the Ministry of Health through its central and regional offices. It mainly targets children aged 0 to 23 months for early childhood vaccinations, including measles vaccination (via the MMR vaccine). It also targets pregnant women (against tetanus) and, as part of specific initiatives, other groups such as young girls against cervical cancer.

The EPI is an ongoing program. Measles vaccination has therefore been a routine intervention since its introduction. The stated objective of the EPI is to eliminate measles and rubella from the country.

Measles and Rubella vaccination steps

The MR vaccine is a live attenuated vaccine, which means it contains weakened versions of the measles and rubella viruses that are unable to cause disease but are capable of stimulating a protective immune response. A single dose is about 95% effective in preventing measles, but two doses are needed for adequate protection against disease, particularly to catch up individuals who may not have responded to the first dose.

As indicated in the schedule of the Expanded Program on Immunization Coordination, the complete vaccination schedule against measles and rubella (MR) consists of two doses in total: a first dose at 9 months and a second dose (or booster) at 15 months. This two-dose schedule is crucial to ensure effective and lasting protection against these diseases.

Target population

From January 2013 to December 2024, the study population consisted of all suspected measles cases that were tested negative in laboratory reported in Côte d'Ivoire within the framework of the national surveillance program. According to the WHO case definition, a suspected measles case is defined as any person presenting a clinician suspected measles, or any person presenting fever and maculopapular rash or any person showing at least one of the following symptoms: coryza, conjunctivitis, or cough. According to the measles diagnostic algorithm, any patient sample confirmed negative for measles should be treated as rubella.

Selection criteria

All patients whose samples tested negative for measles during the period were included in this study. All patients whose samples tested positive for measles and negative measles cases outside the period were not included.

Collection and Transport of Biological Samples

A venous blood sample was collected from each suspected case. The sample collection consisted in 1 to 2 mL for infants and 3 to 5 mL for older children and adults. Blood samples were contained in dry tubes (without anticoagulant) and transported in insulated boxes with ice packs to the reference laboratory. When storage time before analysis is planned to exceed 72 h, a serum was prepared from an aliquot of the sample and stored at -70 °C to preserve antibody integrity.

Detection of Rubella virus antigens'

Detection of measles and rubella specific IgM antibodies was performed at the laboratory using commercial ELISA kits: Anti-Measles Virus IgM and Anti-Rubella Virus IgM ELISA (EUROIMMUN, Lübeck, Germany). Tests were conducted in accordance with the manufacturer's instructions and WHO recommendations for measles and rubella surveillance (EUROIMMUN, 2017; Nardone et al., 2008; Wandinger et al., 2011). Serum samples from suspected measles cases were distributed into microplates pre-coated with specific viral antigens. After incubation and successive washes, bound antibodies were detected using an enzyme-conjugated anti-human IgM labeled with peroxidase. A chromogenic substrate was then added, producing a color intensity proportional to the quantity of antibodies present. Optical density (OD) was measured at 450 nm using a microplate reader, and results (positive, negative, equivocal) were interpreted according to the thresholds defined by the manufacturer. To ensure the reliability and validity of serological results, rigorous quality assurance measures were implemented. Each ELISA run included internal controls provided by the manufacturer (positive and negative controls), in accordance with the EUROIMMUN manual. Results were validated only when these controls met expected performance criteria, according to which, when the absorbance values (OD) of the controls (positive, negative, calibrator) are not within the expected ranges indicated in the batch quality certificate, the test is invalid and must be repeated. (EUROIMMUN, 2017).

Statistical Analyses

The ELISA test results were entered and validated in an EPI-INFO database. The analysis consisted of calculating the IgM positivity rates for measles and rubella by relating the number of confirmed cases to the total number of cases tested. The data were then stratified according to major epidemiological variables: age (groups: 0-11 months, 1-4 years, 5-9 years, 1-14 years, 15-49 years, ≥ 50 years), sex, year of notification, and health region of origin. Comparisons were made between the periods before and after 2018 to identify potential temporal variations associated with the introduction of the MR vaccine. Results were presented as absolute frequencies, proportions (%), and annual trends.

Statistical analyses were performed using R software (version 4.5.1); differences in proportions were assessed using the Chi-square test, with a significance level set at $p < 0.05$.

RESULTS

Between 2013 and 2024, a total of 25,244 serum samples were tested for the detection of rubella-specific IgM antibodies. Of these, 1,463 samples (5.8%) were confirmed positive. The annual distribution of confirmed cases shows notable variations in the positivity rate over the study period. The highest proportions were observed in 2017 (23.1%), 2013

(17.7%), and 2016 (16.2%), reflecting increased viral activity during those years. Conversely, a marked decline in the positivity rate was observed from 2019 onwards, reaching a low in 2022 (0.6%), before rising slightly in 2024 (3.4%). Overall, the data indicate a downward trend in the positivity rate between 2018 and 2024, coinciding with an increase in the number of samples tested. This trend suggests both a gradual reduction in the circulation of the rubella virus and a strengthening of the national surveillance system during this period (Figure 1).

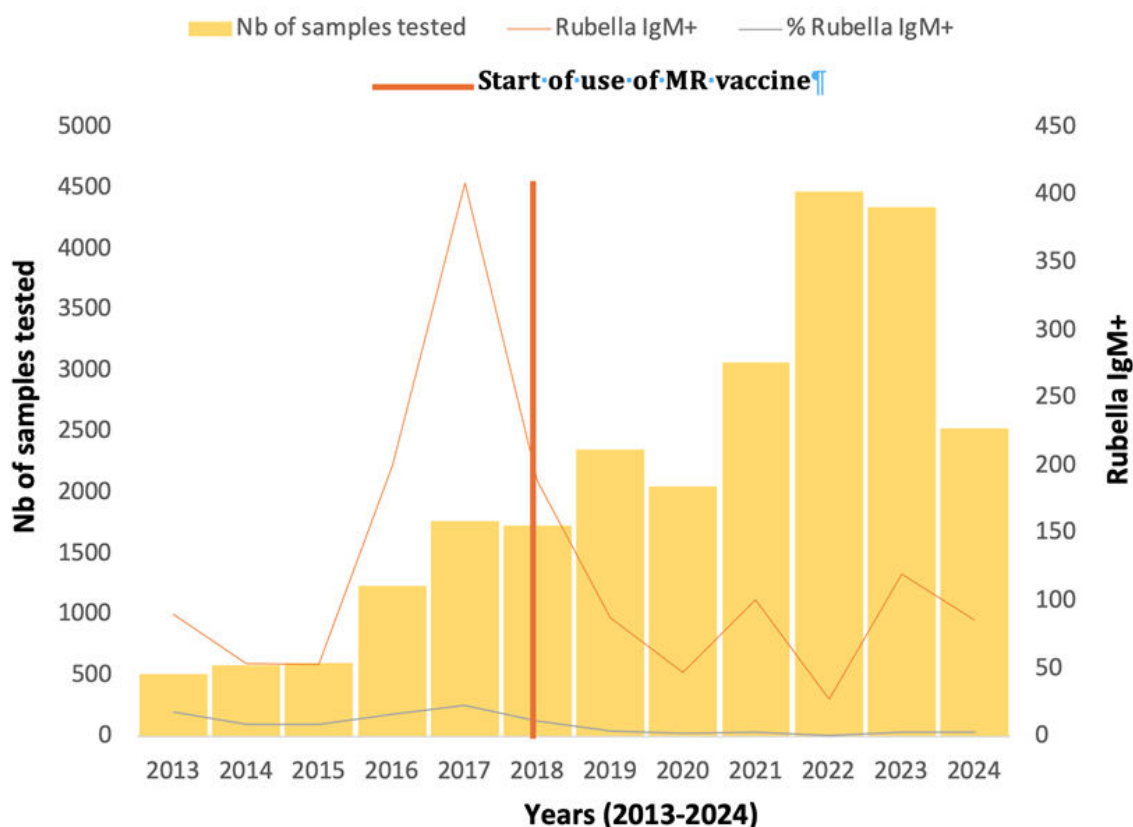


Figure 1: Annual trends in the number of samples tested and rubella IgM positivity in Côte d'Ivoire from 2013 to 2024

Regarding the distribution of cases by age, positivity rates ranged from 3.1% to 6.3% across age groups. The lowest rate was observed in children aged 1 to 4 (3.1%), while those aged 50 and over had the highest proportion (6.3%). Intermediate values were recorded among children aged 10 to 14 (6.1%) and children aged 5 to 9 (4.9%). The chi-square test of independence revealed a highly significant association between age group and serological positivity ($\chi^2 = 53.95$; $df = 5$; $p < 0.001$), indicating that the probability of infection differs significantly according to age (Table 1). These results suggest that virus transmission remains more active among school-aged children and adolescents, while revealing residual circulation among young adults and the elderly, likely related to persistent immune deficits in certain cohorts.

Table 1: Distribution of Rubella IgM Positivity by Age Group in Côte d'Ivoire (2013–2024)

Age group	Samples	Rubella	% Rubella
0-11 months	3151	116	3.7
1-4 years	9141	280	3.1
5-9 Years	4294	210	4.9
10-14 years	1766	107	6.1
15-49 years	1969	90	4.6
≥50 years	126	8	6.3

$$\chi^2 = 53,95 ; \text{ddl} = 5 ; p < 0,001$$

Geographical analysis of confirmed rubella cases reveals a heterogeneous distribution across the country's health districts (Figure 2). Positive cases have been recorded throughout the country, but their frequency varies considerably depending on the geographical area. The highest positivity rates were observed in several urban districts in the south, particularly Abobo-Est, Abobo-Ouest, and Koumassi, which have the highest morbidity rates, with more than 100 cases. Significant transmission has also been

identified in certain districts in the center-west, such as Zoukougbeu, Biankouma, Daloa, and Gagnoa, where positivity rates are significantly higher than in surrounding areas. Conversely, several districts in the north and northeast, including Korhogo, Boundiali, Ferkessédougou, Bondoukou, and Tanda, have significantly lower burdens, generally below 25 cases. Moderate levels are also observed in the southwestern coastal districts, particularly San-Pédro and Tabou. Overall, the geographic distribution of cases shows more intense circulation in densely populated urban areas and certain rural regions in the central-western part of the country, while other districts are experiencing reduced activity. These variations could be related to population density, mobility, and varying performance in detecting and reporting cases.

The analysis of the monthly distribution of rubella positivity between 2013 and 2024 reveals a marked seasonality, characterized by a recurrent peak between February and May, with a median maximum observed in March-April (figure 3). The years 2013, 2016, 2017, and 2018 show the highest values, mainly concentrated in the first half of the year. From 2019 onward, monthly rates drop sharply, reflecting a substantial reduction in viral circulation. The monthly boxplot highlights this trend by showing a consistent seasonal pattern: low values between August and November, a gradual increase beginning in January, followed by a significant peak in the first quarter. This distribution suggests a stable seasonal dynamic, likely influenced by climatic conditions and social interactions typical of the late dry season in Côte d'Ivoire.

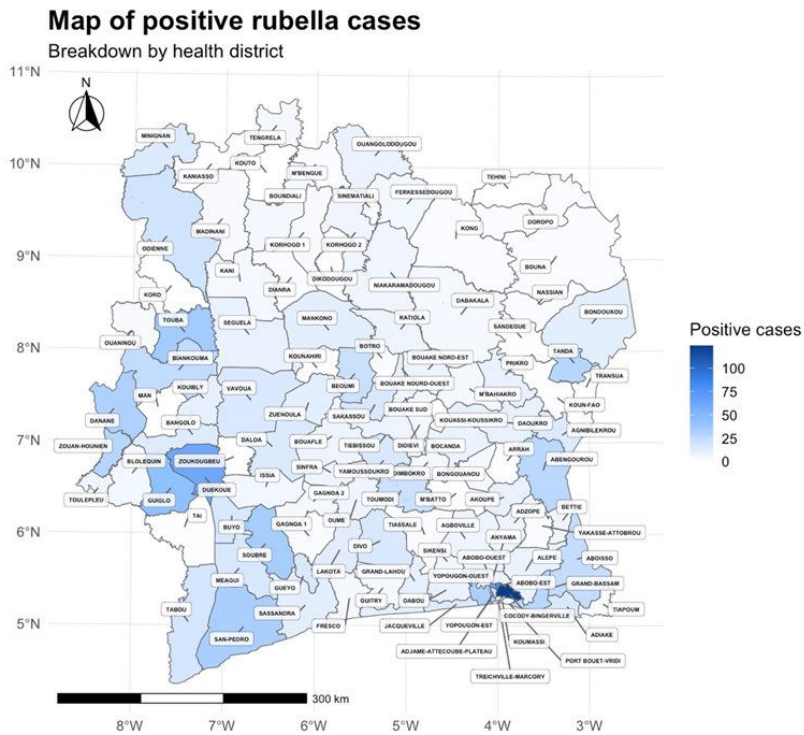


Figure 2: Geographical Distribution of Laboratory-Confirmed Rubella Cases in Côte d'Ivoire (2013-2024)

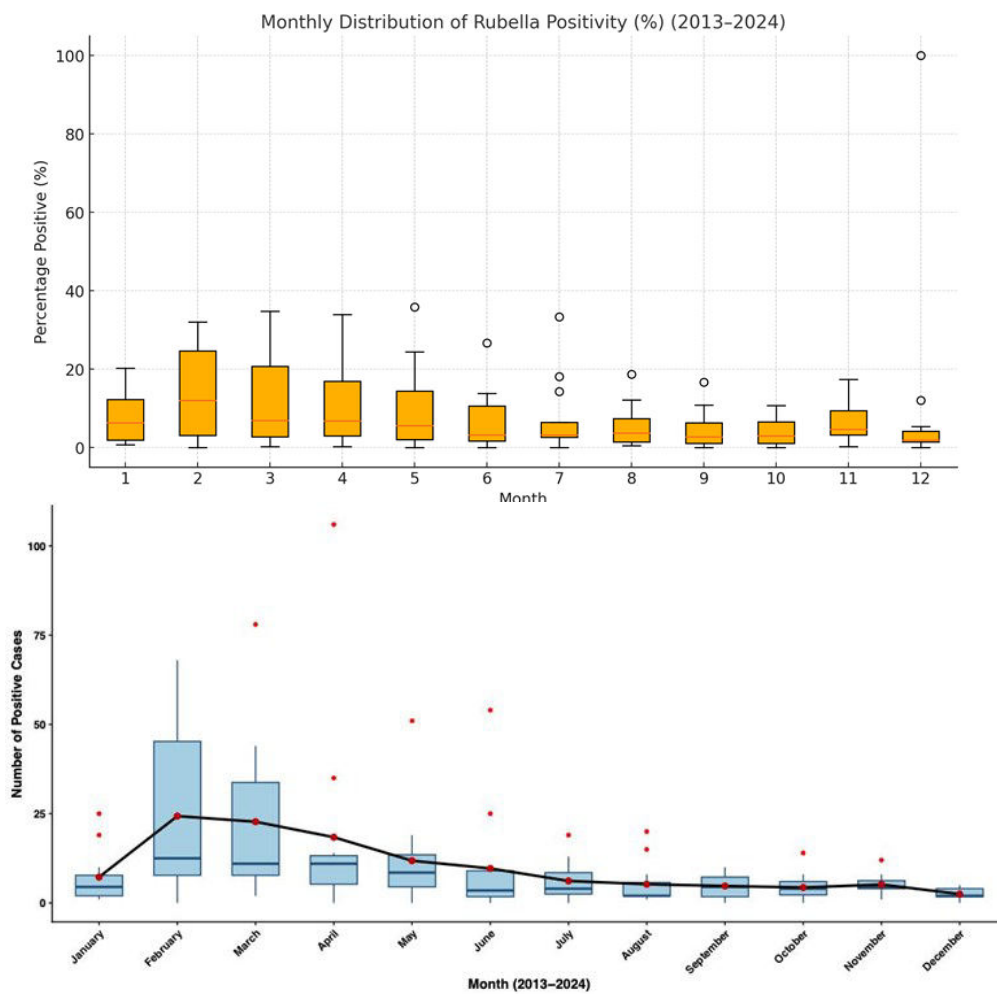


Figure 3 : Monthly distribution of Rubella positive cases over 12 years (2013 – 2024)

Analysis of the contingency table 2 comparing the periods before and after the introduction of the RR vaccine in 2018 shows a very marked decrease in the proportion of rubella-positive cases. Before 2018, the IgM positivity rate was 17.2% (95% CI: 16.1-18.2), whereas after 2018 it was only 3.2% (95% CI: 2.96-3.44). This reduction corresponds to an absolute decrease of approximately 14 percentage points, reflecting a major drop in viral circulation during the post-

vaccination period. The Chi² test, applied to compare the two proportions, reveals a highly significant difference between the periods ($\chi^2 = 1363.1$; $p < 2.2 \times 10^{-16}$). Thus, the probability that this difference is due to chance is extremely low. These results confirm the significant epidemiological impact of the introduction of the RR vaccine, suggesting a substantial decrease in rubella transmission at the national level.

Table 2: Comparison of rubella IgM positivity before and after the introduction of the MR vaccine in Côte d'Ivoire

Period	Number tested	Number positive	Number negative	Proportion positive	95% CI (lower)	95% CI (upper)
Before 2018	4,696	806	3,89	0.1720	0.1610	0.1820
After 2018	20,548	657	19,891	0.0320	0.0296	0.0344

X-squared = 1363.1, df = 1, p-value < 2.2e-16

DISCUSSION

This study is the most comprehensive analysis to date of the epidemiology of laboratory-confirmed rubella over a 12-year period (2013-2024). The results highlight temporal, demographic, and seasonal trends in rubella in Côte d'Ivoire, as well as the significant impact of the introduction of the measles-rubella (MR) vaccine into the expanded program on immunization in 2018. One of the main findings of this study is the marked decrease in rubella antiviral IgM positivity cases after the started use of the MR vaccine in Côte d'Ivoire. This decrease was statistically significant ($\chi^2 = 1363.1$; P-Value < 2.2×10^{-16}), suggesting a major epidemiological impact of the MR vaccine. Similar trends have been observed in other African countries after the introduction of the MR vaccine such as Burkina Faso, Ghana (neighbouring Côte d'Ivoire), Senegal, Rwanda and Tanzania (Luce et al., 2018). Globally, the WHO has also reported a reduction in rubella in regions with vaccination

coverage exceeding 80% (Strebel et al., 2024; Winter et al., 2022).

Analysis of data from Côte d'Ivoire corroborates this downward trend in rubella virus circulation, with a reduction in the positivity rate from 17.2% before the introduction of the vaccine to 3.2% after its introduction. However, the persistence of cases among adolescents and adults demonstrates immune deficiencies, a phenomenon well described in several countries where catch-up campaigns have not covered older cohorts. The absence of extensive catch-up campaigns in Côte d'Ivoire could explain these residual transmissions. The highest positivity rates were observed in children aged 5-14, which has also been reported in other African countries where this age group is considered the main reservoir for rubella transmission (Luce et al., 2018). Notably, the high levels detected in the population aged 50 and over suggest cohorts that have not been previously exposed or immunized;

this phenomenon has also been reported in Zambia (Hayford et al., 2019; Motaze et al., 2020).

The shift in transmission to older age groups is a major public health issue, as it exposes more women of childbearing age to the risk of infection, thereby increasing the likelihood of congenital rubella syndrome. The geographic heterogeneity observed in the distribution of confirmed rubella cases in Côte d'Ivoire suggests the combined influence of demographic, epidemiological, and operational factors. High-density urban districts, such as those in Abidjan, have the highest circulation rates, which is consistent with the well-documented role of population density, mobility, and increased contact frequency in the increased transmission of respiratory viruses, including rubella (Yoshikura, 2014). Studies conducted in other regions in Africa have also shown higher seroprevalence in urban areas, attributed to more intense contact networks (Chimhuya et al., 2015; Getahun et al., 2016). The sustained transmission observed in some districts in the western region may reflect local variations in vaccination coverage and surveillance system performance. Before the widespread introduction of the rubella vaccine in the African Region, the majority of infections occurred at an early age, linked to insufficient herd immunity (Masresha et al., 2025). These geographical differences could also be influenced by unequal access to health services, as documented in several regional analyses (UNICEF, 2023a, 2023b). The geographic heterogeneity observed in the distribution of confirmed rubella cases in Côte d'Ivoire suggests the combined influence of demographic, epidemiological, and other factors. The northern and northeastern districts, where few cases have been detected, may represent areas of low actual circulation, but it is also plausible that under-detection results from logistical constraints and limited access to health services. Caution is therefore needed in interpreting low notifications, in line with the recommendations of the measles-rubella surveillance guidelines for the African Region. Finally, these territorial dispari-

ties underscore the importance of continued strengthening of surveillance and vaccine equity. The introduction of rubella-containing vaccines (RCVs) and the implementation of catch-up strategies targeting unprotected cohorts are essential measures for interrupting transmission and preventing congenital rubella syndrome, as demonstrated by the experiences of several countries that have achieved regional elimination (Plotkin, 2021).

The study shows seasonality characterized by peaks in positivity between February and May. Previous studies conducted in Nigeria and Ghana have reported comparable seasonal dynamics, with increased incidence at the end of the dry season when contact density and the intensity of respiratory infections increase (Durowade, 2022). After 2019, the reduction in the amplitude of seasonal peaks was reported to be due to the introduction of the RR vaccine. However, it should be noted that this period was marked by health measures related to the COVID-19 pandemic, which impacted the circulation of viruses with respiratory tropism (Sullivan et al., 2020). The continuous increase in the number of samples tested since 2019 illustrates a strengthening of the surveillance system in accordance with WHO recommendations. Several regional studies have highlighted the importance of the combined measles/rubella surveillance system for detecting emerging trends (Irons et al., 2003). However, surveillance based primarily on suspected measles cases may underestimate the true burden of rubella, as the vast majority of infections are mild or asymptomatic (Plotkin, 2021). The integration of specific rubella surveillance, supplemented by molecular characterization of circulating strains, could significantly improve understanding of transmission dynamics. The results of this study suggest several priority actions, such as planning catch-up vaccination campaigns, monitoring immunity in women of childbearing age, maintaining high vaccination coverage, and strengthening integrated measles-rubella surveillance.

This study has certain limitations. Passive surveillance based on suspected measles cases may underestimate the actual number of rubella cases due to the high frequency of asymptomatic infections. The lack of individual information on vaccination status limits the causal interpretation of the trends observed. In addition, the downward trends observed between 2020 and 2022 may have been influenced by the COVID-19 pandemic. Despite these limitations, the sample size, the duration of observation, and the systematic laboratory confirmation of cases make the results highly robust.

CONCLUSION

The circulation of rubella in Côte d'Ivoire has decreased significantly since the introduction of the MMR vaccine in 2018, accompanied by improvements in the surveillance system. However, the persistence of cases among school-aged children, adolescents, and some adults highlights immunization gaps that require special attention. Strengthened strategies, including catch-up campaigns and increased surveillance, will be essential to progress toward rubella elimination and reduce the risk of congenital rubella syndrome in the country.

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