

Trends of Measles Hospitalization and Outcome in Northern Nigeria: A Five-Year (2018-2022) Retrospective, Cross-sectional Study

Ibraheem Rasheedat M¹, Ibrahim Olayinka R², Bello Afeez O³, Ogunkunle Taofik O⁴, Aliu Rasaki⁵, Ahmed Kudirat A⁶, Ameen-Ikoyi⁷, Adedeji Omolola N⁸, Suleiman Mohammed B⁹, Hassan Kamiludeen S¹⁰

¹Department of Paediatrics and Child Health, University of Ilorin & University of Ilorin Teaching Hospital, Kwara state, Nigeria. ²Department of Paediatrics, Division of Clinical Medicine, University of Global Health Equity, Kigali, Rwanda. ³Department of Paediatrics, Federal Medical Centre Bida, Niger state, Nigeria. ⁴Dalhatu Araf Specialist Hospital, Lafia, Nasarawa state & International Foundation against Infectious Disease in Nigeria, FCT Abuja, Nigeria. ⁵Department of Paediatrics, Gombe State University & Federal Teaching Hospital Gombe, Gombe state, Nigeria. ⁶Kaduna State University & Barau Dikko Teaching Hospital Kaduna, Kaduna state, Nigeria. ⁷Department of Paediatrics & Child Health, University of Ilorin Teaching Hospital, Ilorin, Kwara state, Nigeria. ⁸Department of Paediatrics & Child Health, University of Ilorin Teaching Hospital, Ilorin, Kwara state, Nigeria. ⁹Department of Paediatrics, Federal Medical Centre Katsina, Katsina state, Nigeria. ¹⁰Department of Paediatrics, Gombe State University & Federal Teaching Hospital Gombe, Gombe state, Nigeria.

Abstract

Background: The coronavirus disease-2019 (COVID-19) negatively affected vaccination rates, increasing measles cases in Nigeria. Severe cases managed at referral centres particularly require documentation. This study compares the pre-COVID and COVID-time burden and outcomes of hospitalized children with measles in North Nigeria. **Material and Methods:** A descriptive cross-sectional, retrospective study involving hospitalized children with measles from January 1, 2018 to December 31, 2019 (pre-COVID time) and January 1, 2020 to December 31, 2022 (COVID-19 time) at six tertiary facilities in northern Nigeria. Data on demographics, vaccination status and hospitalization outcome were collected. **Results:** Out of 45,056 hospital admissions, 468 were measles cases (1.0% incidence); 79 measles cases pre-COVID-19 years and 389 during the COVID-19 years. Among these, 405 (86.6%) were under-fives, and 261 (55.8%) were male. The odds of measles occurrence during the COVID-19 years were 2.9 times higher (95% C.I.: 2.3-3.7). The proportion of hospitalized under-five patients remained stable (87.5% in 2018 to 86.7% in 2022, $P=0.513$), and most patients (333, 71.2%) were unvaccinated. The case fatality was 15.4% (72/468), rising from 0.0% in 2018 to 21.8% in 2022 ($P=0.001$). Mortality odds during COVID-19 years were 8.4 times higher than pre-COVID-19 (95% C.I.: 2.0-35.2) time. **Conclusion:** The proportion of hospitalized children under five with measles remained constant. However, the mortality rate during the COVID-19 years compared to pre-COVID years was higher, particularly among the under-fives. Many children remain unvaccinated, stressing the need to close immunization gaps and address vaccine hesitancy.

Keywords: Admission outcome, Children, COVID-19, Hospitalization, Measles, Nigeria.

Received: 25 May 2025

Revised: 20 June 2025

Accepted: 20 August 2025

Published: 19 September 2025

INTRODUCTION

Measles, a highly contagious viral infection, poses significant morbidity and mortality risks, especially in unvaccinated children.^[1] The global impact of measles has been greatly reduced due to effective vaccination, with the World Health Organization (WHO) reporting over 23 million deaths averted annually between 2000 and 2018.^[2] Indeed, before vaccine advent, measles-related deaths exceeded 2.6 million, dropping to about 90,000 in 2016.^[2]

Despite global progress, Nigeria, particularly in the northern region, still faces recurrent measles outbreaks, exacerbated by low immunization coverage and a previous reliance on a single vaccine dose instead of the recommended two.^[3-5] The COVID-19 pandemic worsened this situation, disrupting vaccination programs due to lockdowns, health facility closures, and resource reallocation.^[6-8] Consequently, Nigeria experienced a measles outbreak in March 2020, with 908 cases reported across 16 states.^[9] The primary objectives of this study were to determine and compare the incidence and hospitalization outcomes (survival or death) of children

hospitalized with measles during the pre-COVID-19 and COVID-19 periods. The secondary objectives were to analyze and compare the vaccination status of these children across the two periods.

MATERIALS AND METHODS

Study design: This study was a descriptive cross-sectional retrospective study. Data for five years (2018 till 2022) was collected from six sites, and the duration of January 1, 2018 to

Address for correspondence: Dr. Rasheedat M. Ibraheem, Department of Paediatrics and Child Health, University of Ilorin & University of Ilorin Teaching Hospital, Kwara state, Nigeria. E-mail: ibraheem.rm@unilorin.edu.ng

DOI:
10.21276/amt.2025.v12.i3.61

How to cite this article: Rasheedat MI, Olayinka RI, Afeez OB, Taofik OO, Rasaki A, Kudirat AA, -Ikoyi A, Omolola NA, Mohammed BS, Kamiludeen SH. Trends of Measles Hospitalization and Outcome in Northern Nigeria: a Five-Year (2018-2022) Retrospective, Cross-sectional Study. *Acta Med Int.* 2025;12(3):194-199.

the December 31, 2019 was categorised as the pre-COVID-19 time, while January 1, 2020 till December 31, 2022 was categorised as the COVID-19 time.

Study setting: The study sites spanned all three geopolitical zones in northern Nigeria, consisting of three tertiary health institutions from the North-Central Region, two centres from the North-West Region, and a centre from the Northeast Region. In the northwest (NW), the study sites were the towns of Katsina and Kaduna in Katsina and Kaduna State, respectively. For the North-Central Region (NC), in Bida, Niger State, Ilorin, Kwara State and Lafia in Nasarawa State, while in the Northeast Region (NE), Gombe town in Gombe State.

Northern Nigeria consists of 19 states within the three geopolitical regions with an estimated population of 104 million based on the 2016 projections of the 2006 national census.^[10] According to the 2018 Nigeria Demographic Health Survey, Northern Nigeria had the least proportion of fully immunized children in Nigeria, ranging from 11.3% and 20.0%.^[11] The proportion of children aged 12-23 months who received a dose of measles vaccine also ranged from 39.1% in NW, 43.3% in NE, and 54.2% in NC.^[11]

Sample size: All children hospitalized with measles who fulfilled the eligibility criteria were enrolled. The eligibility criteria were any child aged 14 years and younger with a clinical diagnosis of measles infection according to the WHO definition for clinical measles with or without laboratory confirmation who was admitted between January 1, 2018, and December 31, 2022. Exclusion criteria included outpatients with measles, and those with other forms of viral exanthems.

Data collection method: Records of all children admitted to the Emergency Paediatrics Unit/Ward at the study sites between January 1, 2018, and December 31, 2022, were obtained from the admission registries. These registries include information such as hospital number, name, gender, address, admission date, diagnosis, hospital stay outcome, and discharge date for all admitted children. Nurses and doctors update the registers daily. Hospital numbers were then used to retrieve case folders for additional details, including the child's vaccination status. A child's vaccination status was classified as fully vaccinated if they had received at least one dose of the measles vaccine or had a certificate of full vaccination, partially vaccinated if they had received some vaccines but not the measles vaccine, and unvaccinated if they had not received any vaccines. The hospitalization outcome for each child was recorded as either survived or died. Data collection occurred between the March 1, and September 30, 2023.

Statistical analysis: The data recorded on the proforma were entered into Microsoft Excel using numerical codes and analyzed with IBM® Statistical Package for the Social Sciences (SPSS) version 23.0 (Chicago, Illinois, USA). The proportion of children with measles, deaths and survivors, were reported as frequencies and percentages. Continuous variables, such as the subjects' ages, were presented as mean (standard deviation, SD), median, or interquartile range, depending on the data distribution. Associations between demographic data and outcome parameters were assessed

using a chi-square test. A P value of less than 0.05 was considered statistically significant.

Ethical permission and patient consent: Approval for the study was granted by the Health Research Ethical Review Committee of the institution (UITH_ERC_PAN/2023/02/0355) before the data extraction process began. The committee waived the need for informed consent due to the retrospective nature of the medical record review, and there was no patient contact. The participants' anonymity was preserved during data collection.

RESULTS

Demographic characteristics of the study children

A total of 468 patients with measles were admitted to six tertiary health facilities in northern Nigeria. The median age of these patients was 21.0 months, with an interquartile range of 12.0 to 36.0 months and the minimum age of five months to a maximum of 156 months. Among them, 261 (55.8%) were male, and the age distribution was similar between the sexes, [Table 1].

Incidence of measles

In the five-year period, there were 468 cases out of 45,056 admissions across the six tertiary health facilities with an incidence of 1.0% (giving an incidence of 10 cases per 1000 admission cases). The incidence ranged from 0.7 to 1.3% across the health facilities [Table 2].

Trends in measles admissions

During the five-year period, the proportion of admitted patients with measles increased from 0.2% in 2018 to 2.6% in 2022, which corresponds to a 400.0% increase from baseline (2018), with a chi-square for trends of 365.28, $P < 0.001$ (Table 3). There were 79 measles cases from 2018 to 2019 (pre-COVID-19) and 389 cases from 2020 to 2022 (COVID-19 period) (Table 3). The odds of measles occurrence during the COVID-19 interval was 2.92 (95% C.I.: 2.29 to 3.73, $P < 0.001$) compared to the pre-COVID interval.

Based on the age groups, 405 (86.5%) were children less than five years old; the percentage of children under five years old remained fairly the same from 2018 to 2022 as shown in [Figure 1]. The chi-square for trends was 3.73, $P = 0.513$.

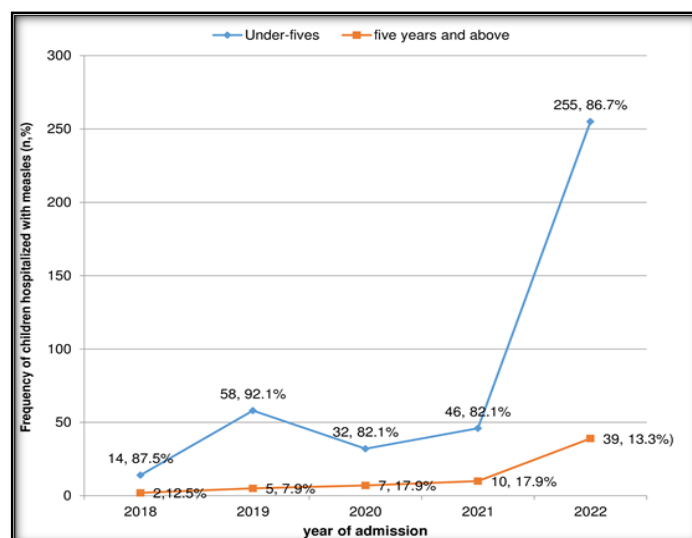


Figure 1: Trends of measles infection based on the age groups among the study participants

Based on the monthly distribution, the peak cases occurred in April, with the lowest cases recorded in October [Figure 2].

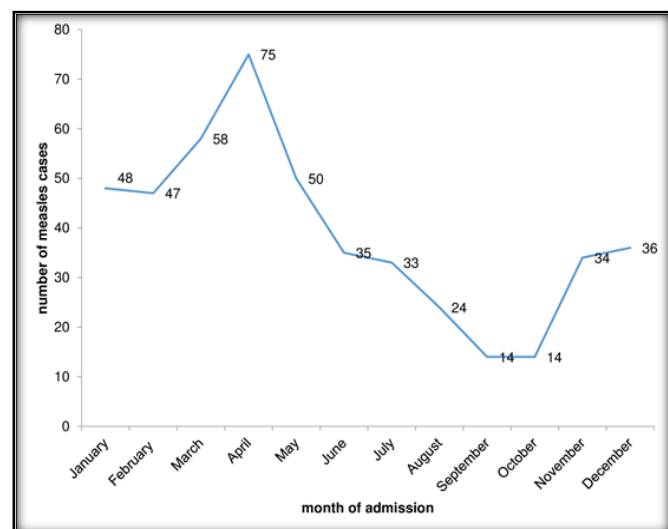


Figure 2: Monthly distribution of measles cases among the study children

Trends in vaccination status among the study participants: Of the 468 children in the study, 333 (71.2%) were unvaccinated, 59 (12.6%) were partially vaccinated, and 76 (16.2%) were fully vaccinated. The percentage of patients who were not vaccinated among those hospitalized with measles decreased from 100.0% in 2018 to 69.4% in 2022, [Figure 3], with a chi-square trend of 11.343 ($P=0.023$). The odds of a child likely not receiving the measles vaccine pre-COVID-19 period compared with the COVID-19 era were not significantly different (OR 1.34, 95% CI: 0.77 to 2.35).

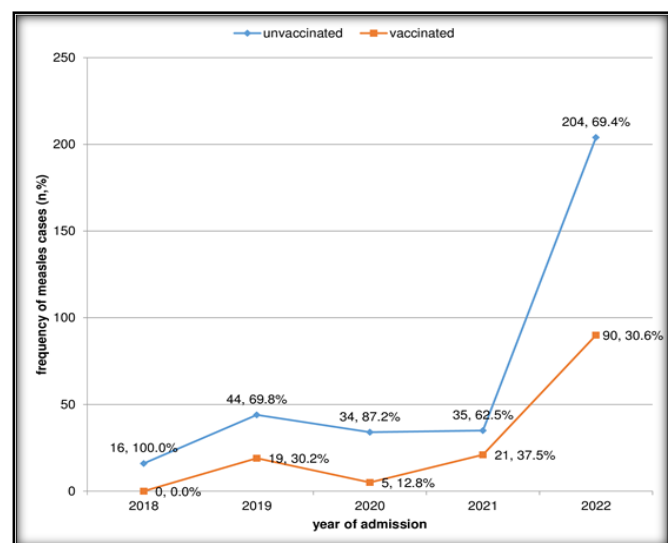


Figure 3: The trends in measles vaccination status among the study children

Trends in outcomes of hospitalized children with measles
Among the 468 children hospitalized with measles, 72 died,

with a case fatality rate of 15.4%; 39 (54.2%) were females, and 33 (45.8%) were males ($P=0.065$). The majority of the deaths occurred in the under-five group (67, 93.1%). The mortality trend increased from 0.0% in 2018 to 21.8% in 2022 [Figure 4], with a chi-square value of 23.36 ($P=0.00112$). The odds of death during the COVID-19 period compared with the pre-COVID-19 period were 8.45 (95% CI: 2.03 to 35.21). The chi-square for trends showed a progressive increase in death with increasing measles cases, with a chi-square for the trend of 18.65, $P=0.00092$.

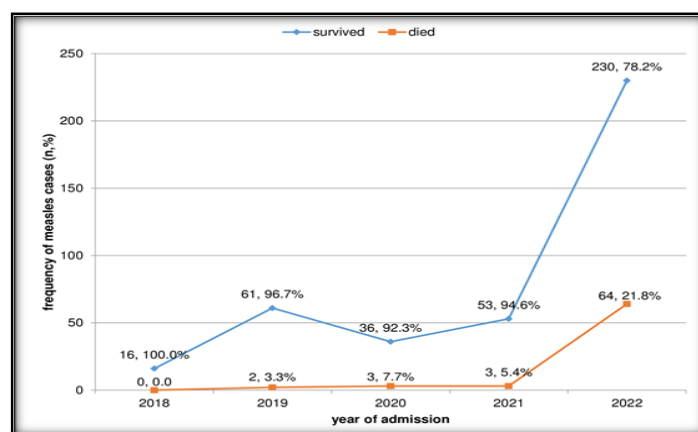


Figure 4: Trends of hospitalization outcomes (death) among the study children

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Chairman: OLOROGUN O'TEGA EMERHOR (JCHC)

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Fellow (NIGCAL), Fellow (ICMA) England.

Old Jebba Road, Oke-Ose,
P.M.B. 1459, Ilorin,
Kwara State, Nigeria.
Website: www.uithilorin.org.ng
Email: info@uithilorin.org.ng
Telephone: 08055763942

UITH ERC Protocol Number: ERC-PH/2022/PW/113
UITH ERC Approval Number: ERC-PH/2022/02/053

Our Ref: UITH/CAT/189/21st/376 Date: 07/02/2023

A COMPARISON OF THE PRE-COVID AND COVID CLINICAL PRESENTATION OUTCOME OF MEASLES INFECTION AMONG HOSPITALIZED CHILDREN IN NORTHERN NIGERIA.
UITH Ethical Research Committee (ERC) assigned number: NHREC 02/05/2010
Name of Applicant/Principal Investigator: Dr Ibraheem R.M & Co
Address of Applicant: Dept. Of Paediatrics, University Of Ilorin Teaching Hospital, Ilorin/UNILORIN
Date of receipt of application: 02/05/2022
Type of Review: Full Committee Review
Date of full Committee Decision on the Research: 27/09/2022
Date of full Committee approval: 07/02/2023

Notice of full Committee Approval
I am pleased to inform you that the research described in the submitted protocol, the consent forms and other participant information materials have been reviewed by the UITH Ethical Review Committee (ERC) and given full Committee approval.

This approval dates from 08/02/2023 to 07/02/2024. You are requested to inform the committee at the commencement of the research to enable it appoint its representative who will ensure compliance with the approved protocol. If there is delay in starting the research, please inform the ERC so that the dates of approval can be adjusted accordingly.
Note that no participant accrual or activity related to this research may be conducted outside these dates.

The UITH ERC requires you to comply with all the institutional guidelines and regulations and ensure that all adverse events are reported promptly to the ERC.
No changes are allowed in the research without prior approval by the ERC. Please note that the ERC reserves the right to conduct monitoring/oversight visit to your research site without prior notification. Notwithstanding above, we will not be responsible for any misconduct on the part of the researcher in the course of carrying out the research.
Thank you

PROF. P. O. AJIBOYE MBBS, MPhil, PhD, FRCR
Chairman, UITH Ethics Review Committee (NHREC)

IRB approval.

Table 1: The demographic characteristics of the study participants

Age group	Total n (%)	Male n (%)	Female n (%)	P value
≤ 12 months	143 (30.6)	89 (34.1)	54 (26.1)	0.056
13 – 59 months	262 (56.0)	144 (55.2)	118 (57.0)	
≥ 60 months	63 (13.5)	28 (10.7)	35 (16.9)	
Total	468 (100.0)	261 (100.0)	207 (100.0)	

Table 2: Incidence of measles infection across health facilities

Facility Location	Number of overall admissions	Frequency of Measles cases	Incidence (%)
Kaduna	5747	74	1.3
Katsina	8652	83	1.0
Nasarawa	7246	75	1.0
Niger	10065	75	0.8
Kwara	7553	88	1.2
Gombe	5793	40	0.7
Total	45056	468	1.0

Table 3: Trends in the incidence of measles cases from 2018 to 2022 among the study participants

Parameter	Number of overall Admissions N=45056	Frequency of Measles cases N=468	Percent contribution of measles cases
Year			
2018	7843	16	0.20
2019	8845	63	0.71
2020	8556	39	0.46
2021	8415	56	0.67
2022	11397	294	2.58
Timing			
Pre-COVID-19	16688	79	0.47
COVID-19	28368	389	1.37

DISCUSSION

This study focused on trends in hospitalized measles patients in the immediate pre- and post-COVID-19 eras. Measles remains one of the leading causes of death in children,^[5] and recognizing this trend will further assist in understanding the measures and policies needed to minimize measles and attain global targets. Measles infection accounted for between 0.7 and 1.3% of admissions in the six selected hospitals in northern Nigeria. This finding is much greater than the findings from a recent Somali study in which measles accounted for 0.1% of hospital admissions.^[12] Indeed, our study's findings are inconsistent with measles control efforts, as most of the states in the study conducted measles vaccination campaigns (MVC) in 2019, 2021 and 2022. These MVC play a significant role in measles control as these campaigns often target areas with outbreaks and target children who have either missed the initial vaccination, or didn't develop antibodies for protection. Indeed, Nigeria has conducted measles supplemental immunization activities (SIA) every two years since 2005 intending to provide an additional opportunity for vaccination.^[13]

Male children constituted 55.8% of admissions for measles in this study, while the majority (86.5%) were under-five children, which is consistent with findings from some hospital-based studies and surveillance reports.^[14-17] Fewer cases were observed in individuals aged five years and above, which was expected since most in this age group are likely to have been exposed to the measles antigen, either through vaccination or prior infection, and have developed immunity to the virus.^[18,19]

Our study showed a 400% rise in the number of measles patients admitted to hospitals between 2019 and 2022. This

finding implies that more cases of measles were detected immediately following the COVID-19 pandemic. A report by the Global Alliance for Vaccine and Immunization in 2022 identified 15 (22 to 37) countries with outbreaks of measles from 2021 to 2022.^[20] These increased outbreaks accounted for 18% more infections of measles reported globally,^[20] and were attributed to setbacks with surveillance and immunization efforts in the affected countries.

Measles cases primarily occurred during the dry, cold Harmattan season, with peak hospital admissions in the first quarter of the year, followed by a decrease as the rainy season began. Similar findings were reported in earlier Nigerian studies of measles outbreaks, with an increasing incidence during the Harmattan in March or April.^[14,16,19,21-23] Usually, during outbreaks or to prevent further outbreaks, supplemental immunization activities and vaccination weeks are undertaken to target all eligible children irrespective of their vaccination status,^[24,25] but there is a need to maintain routine vaccination during this activity period and throughout the year to maintain herd immunity.^[26]

The advent of COVID-19 had a great deal of impact on vaccination targets globally. At the peak of the pandemic, resources were reallocated to cater to exigencies related to COVID-19, and some health facilities were closed during this period.^[6] In our study, only 76 (16.2%) of the patients with measles were fully vaccinated, and indeed, the trend of vaccination decreased steeply from 100.0% in 2018 to 69.4% in 2022. This finding may indicate a decline in immunization coverage in the northern states where these hospitals are domiciled. Indeed, the low vaccination status found in the current study despite MVC in 2021 could be attributable to vaccine hesitancy, one of the major drivers of measles in Nigeria.^[27] Lacobucci et al reported that approximately 40 million children

in total missed one of the two recommended doses of the measles vaccine in 2021 globally.^[28] These findings further buttress that this is a global challenge that stakeholders need to pay attention to. The adoption of strategies, including raising public awareness and increasing community involvement, boosting routine immunization services, tackling vaccine hesitancy, enhancing disease surveillance and notification systems, managing socioeconomic health determinants, and promoting multi-sectoral engagement and coordination has been recommended.^[27]

The mortality rate associated with measles has increased recently, with 136,000 deaths reported in 2022, which is a 43% increase compared to the 2021 mortality rate.^[6] Our study also revealed this worsening mortality, as evidenced by the increase in measles mortality, with 64 deaths occurring among 230 patients in 2022. Our study also revealed an increase in mortality from 5.4% to 21.8% when comparing the mortality of measles patients in 2021 and 2022, respectively. The fact that most measles deaths occur in those under five years old has been reported by the WHO,^[1] and earlier studies.^[14–17] The observation of higher mortality in females compared to males in the current study may be partly linked to the healthcare-seeking behaviours of mothers in the country. It has been noted that mothers often seek medical advice and care for their male children more frequently than for their female children,^[29] leading to delays in treatment for girls.^[30]

This study has the strengths of being a multicenter study, and each geopolitical zone in northern Nigeria had at least one representative hospital. The limitations of the current study include data retrieval challenges due to poor standardization of the records in the studied centres. The need for all tertiary health institutions to embrace electronic medical records to enhance data management in these hospitals is crucial.

CONCLUSION

In conclusion, this study highlights the trends in measles cases and mortality in northern Nigeria, with a significant surge in cases following the COVID-19 time compared to the pre-COVID time. This study revealed increased measles-related mortality, especially among people under five years of age, emphasizing the need for improved healthcare access and awareness. Despite, previous measles vaccination campaigns, a large proportion of children still remain unvaccinated. Hence, prompt closure of immunization gaps and addressing of vaccination hesitancy is crucial.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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