

# Comparative seroprevalence of measles virus immunoglobulin M antibodies in children aged 0–8 months and a control population aged 9–23 months presenting with measles-like symptoms in selected hospitals in Kaduna State

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**Background:** Measles remains the leading cause of vaccine-preventable childhood mortality in developing countries, with its greatest incidence in children younger than 2 years of age. The aim of this study was to determine the seroprevalence of measles virus in children (aged 0–8 months) and older children (aged 9–23 months) presenting with measles-like symptoms.

**Methods:** A total of 273 blood samples comprising 200 from children aged 0–8 months and 73 from children aged 9–23 months were collected and analyzed for measles virus IgM antibodies by enzyme-linked immunosorbent assay.

**Results:** An overall prevalence of 21.2% was obtained, with a prevalence of 6.5% in children aged 0–8 months and 61.6% in children aged 9–23 months. The prevalence of measles virus increased with age in children aged 0–8 months and decreased with age in older children (aged 9–23 months), showing a significant association between measles virus and age of the child ( $P=0.000$ ). A higher prevalence was found in females (27.5%) than in males (16.3%) and this difference was significant (odds ratio 1.942,  $P=0.025$ ). There was no significant association with the level of parental education, parental occupation, or number of children in the family ( $P>0.05$ ). With respect to children's vaccination status and breastfeeding, there was a significant association ( $P<0.05$ ). The marital status of the family, place of residence, and household size showed no significant association with the prevalence of measles virus. However, a significant association was observed in relation to maternal measles history (odds ratio 2.535,  $P=0.005$ ) and maternal vaccination status (odds ratio 1.791,  $P=0.049$ ), as well as between measles virus infection and all presenting symptoms, except for vomiting, malaria, typhoid, and pneumonia, which showed no significant association ( $P>0.05$ ).

**Conclusion:** The findings of this study confirm the presence of measles virus infection in children aged 0–8 months.

**Keywords:** measles virus, malaria, vaccination, breastfeeding

## Introduction

Measles, also known as rubeola, is an infection of the respiratory system caused by measles virus (MV), a spherical, enveloped, single-stranded, negative-sense RNA virus.<sup>1</sup> It is transmitted primarily from person to person by large respiratory droplets, but can also be spread by aerosolized droplets<sup>1</sup> as well as close personal contact or direct contact with nasal or throat secretions from infected persons.

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Measles is most infectious during the prodrome phase. The prodromal period begins with fever, malaise, cough, coryza, and conjunctivitis. Koplik spots appear on the buccal mucosa 1–2 days before rash onset and may be noticeable for an additional 1–2 days after rash onset. In developed countries, the most commonly cited complications associated with measles infection are otitis media, pneumonia, post-infection encephalitis, subacute sclerosing panencephalitis, and corneal ulceration (leading to corneal scarring). The risks of serious complications and death are increased in young children and adults. Complications are usually more severe in adults.<sup>2</sup>

Measles occurs worldwide, and is still a significant cause of childhood morbidity and mortality despite the existence of an effective vaccine. It is a highly infectious immunization-controllable disease, but is still responsible for high mortality among children, particularly in developing nations, including Nigeria, where it is still endemic.<sup>3,4</sup> After an effective measles vaccine was introduced in 1963, the incidence of measles decreased significantly. Vaccination coverage of measles-containing vaccine in Nigeria according to the World Health Organization (WHO)/United Nations Children's Fund is currently put at 62%. The National Program on Immunization in Nigeria stipulates that children be vaccinated against measles by a single injection at 9 months. This is because children below this age are believed to possess passively acquired maternal antibodies that protect them against the virus. However, in developing countries where measles is highly endemic, the WHO recommends two doses of vaccine be given at 6 and 9 months of age.<sup>5</sup>

The aim of this study was to determine the seroprevalence of MV in children aged 0–8 months as compared with older children (9–23 months) presenting with measles-like symptoms at selected hospitals in Kaduna State. It also sought to determine some sociodemographic and possible risk factors associated with the infection.

## Materials and methods

### Study area and population

The study was conducted in three major hospitals in Kaduna State, including Hajia Gambo Sawaba General Hospital, Kofar-Gayan, located in the Zaria Local Government Area, and Yusuf Dantsoho Memorial Hospital and Gwamna-Awan Hospital, both located in Kaduna metropolis. The study population included children aged 0–8 months presenting with measles-like symptoms and attending the hospitals selected for the study. These symptoms include fever, cough, coryza, conjunctivitis, diarrhea, vomiting, rash, and Koplik spots, as well as some non-specific symptoms characteristic of

typhoid fever, pneumonia, and malaria. Children aged 9–23 months presenting with measles-like symptoms and attending the hospitals were used as the control population. Ethical approval was obtained from the ethics committee at Kaduna State Ministry of Health. The purpose and procedure of the study were explained to the parents or caregivers and their consent was obtained before enrollment in the study.

### Sample size

The sample size was determined using the following equation of Naing et al:<sup>6</sup>

$$n = \frac{Z^2 pq}{d^2}$$

where  $n$  is the sample size;  $Z$  is the standard normal distribution at a 95% confidence interval of 1.96;  $p$  is the prevalence (8%<sup>7</sup>);  $q = 1 - p$ ; and  $d$  is the absolute desired precision (0.05). Therefore:

$$n = \frac{(1.96)^2 \times 0.08 \times (1 - 0.08)}{(0.05)} = 113.10 = 113.10 \text{ samples}$$

However, a total of 292 samples were collected for the study and distributed in a ratio of 3:1 to arrive at 219 for children aged 0–8 months (study population) and 73 for children aged 9–23 months (control population). However, 19 samples were not suitable for assay, being lipemic, and were discarded, giving a total of 273 samples. Of the 273 samples assayed, 200 were from children aged 0–8 months (study population) and 73 were from children aged 9–23 months (control population).

### Sample collection and processing

Using a sterile disposable syringe, a 2 mL blood sample was collected from each patient aseptically by venipuncture and dispensed into sterile, labeled, anticoagulant containers containing ethylenediaminetetraacetic acid. The blood samples were transported in an ice box to the laboratory. The blood samples were allowed to settle and the plasma was separated using clean Pasteur pipettes into sterile plain sample containers. The samples were stored at refrigeration temperature (4°C) until required for analysis.

The samples were analyzed using immunoglobulin M measles enzyme-linked immunosorbent assay reagent (Diagnostic Automation and Cortez, Calabasas, CA, USA). All samples and reagents were removed from the refrigerator and allowed to come to room temperature (25°C). The coated

strips were placed in a holder and labeled (one blank well, one negative control, two calibrators, one positive control, and 91 wells for sample specimens). About 3  $\mu$ L of the test samples, negative control, positive control, and calibrators, was added to 240  $\mu$ L of the serum diluent and mixed well to make 1:80 dilutions. Next, 100  $\mu$ L each of the diluted samples was dispensed into appropriate wells, ensuring that there were no air bubbles. Air bubbles present in the liquid were removed by tapping the holder, and 100  $\mu$ L of the serum diluent was then added into the reagent blank well. The wells were incubated at room temperature (21°C–25°C) for 30 minutes. After incubation, the liquid from all wells was removed by washing three times with 300  $\mu$ L of wash buffer. Next, 100  $\mu$ L of enzyme conjugate was added into each well and incubated at room temperature for 30 minutes. Excess enzyme conjugate was removed by washing three times with the buffer; 100  $\mu$ L of chromogen/substrate solution was then dispensed into each well and incubated at room temperature for 15 minutes. The reaction was stopped by addition of 100  $\mu$ L of stop solution (1 M  $H_2SO_4$ ) and the plate was tapped gently to mix the contents of the wells. The reading was done using an enzyme-linked immunosorbent assay microplate reader at 450 nm.

## Statistical analysis

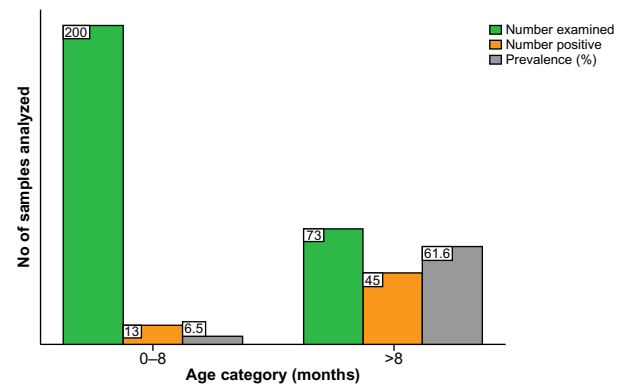
Data generated from questionnaires and results obtained from laboratory analysis were entered into Microsoft Excel. The data obtained were analyzed using Statistical Package for the Social Sciences version 20.0 software (IBM Corporation, Armonk, NY, USA). The Pearson's Chi-square test was used to determine the significance of variables at a 95% confidence interval, and a  $P$ -value  $<0.05$  was considered to be statistically significant. The odds ratio (OR) was used to measure association for 2 $\times$ 2 contingency tables and an OR  $>1$  was taken as a positive association. Side-by-side bar charts were used to visually display the results of cross-classification data for disease prevalence.

**Table 1** Seroprevalence of measles virus infection in children in relation to hospital location

Hospital	Examined (n)	Positive (n)	Prevalence (%)	$P$ -value
GAH	79	10	12.7	0.086
YDMH	112	28	25.0	
HGSGH	82	20	24.4	
Total	273	58	21.2	

**Note:**  $\chi^2=4.910$ ,  $df=2$ ,  $P=0.086$ .

**Abbreviations:** GAH, Gwamna-Awan Hospital; YDMH, Yusuf Dantsoho Memorial Hospital; HGSGH, Hajia Gambo Sawaba General Hospital.



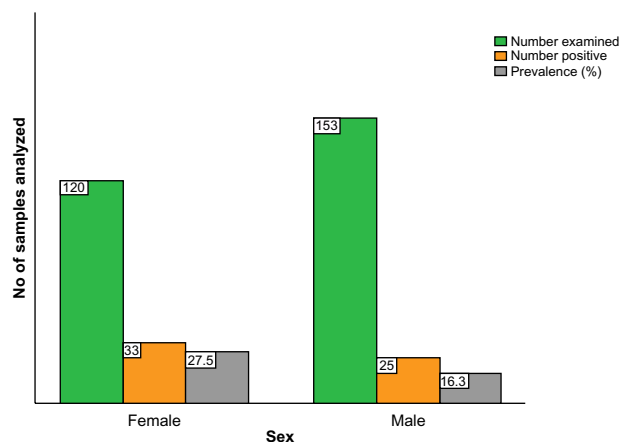
**Figure 1** Seroprevalence of measles virus infection in children in relation to their age category ( $\chi^2=97.195$ ,  $df=1$ , odds ratio 23.118,  $P=0.00$ ).

## Results

The prevalence of MV immunoglobulin M antibodies obtained in this study was 21.2%, with Yusuf Dantsoho Hospital having the highest prevalence (25%), followed by Hajia Gambo Sawaba General Hospital (24.4%), and Gwamna-Awan Hospital, which had the lowest prevalence (12.7%, Table 1).

Children aged 0–8 months had a prevalence of 6.5%, but the prevalence was significantly higher in children aged older than 8 months (61.6%), showing a significant association between MV infection and age of the child ( $P=0.00$ , Figure 1). The prevalence was also significantly higher in female children (27.5%) than in male children (16.3%) indicating a possible association between MV infection and sex of the child ( $P=0.025$ , Figure 2).

The parents' sociodemographic data were assessed in relation to MV infection in their children. There was no significant association between MV infection and level of parental education ( $P=0.687$ ), occupation of parents ( $P=0.207$ ), or number of children in the family ( $P=0.828$ , Table 2).



**Figure 2** Seroprevalence of measles virus infection in children in relation to their sex ( $\chi^2=5.006$ ,  $df=1$ , odds ratio 1.942,  $P=0.025$ ).

**Table 2** Seroprevalence of measles virus infection in children in relation to parental sociodemographic data

Factors	Examined (n)	Positive (n)	Prevalence (%)	P-value
Educational status				
Primary	107	26	24.3	0.687
Secondary	88	17	19.3	
Tertiary	43	7	16.3	
Other	35	8	22.9	
Occupation				
Housewife	115	28	24.3	0.207
Self-employed	126	21	16.7	
Civil servant	32	9	28.1	
Children (n)				
1–3	129	25	19.4	0.828
4–6	105	25	23.8	
7–9	32	7	21.9	
>9	7	1	12.1	

**Notes:** Educational status,  $\chi^2=1.480$ ,  $df=3$ ,  $P=0.687$ ; occupation,  $\chi^2=3.146$ ,  $df=2$ ,  $P=0.207$ ; number of children,  $\chi^2=0.891$ ,  $df=3$ ,  $P=0.828$ .

The study established a significant association between MV infection and the child's vaccination status ( $P=0.031$ ), with vaccinated children having a lower prevalence (10.0%) than unvaccinated children (23.8%). There was also a significant association between MV infection and breastfeeding babies ( $P=0.000$ , Table 3). The findings did not establish any significant association in relation to type of family ( $P=0.716$ ), place of residence ( $P=0.966$ ), or number of persons living in the household (Table 4).

There was a significant association between MV infection in children and maternal measles history ( $P=0.005$ ). Children of mothers with a past history of measles had a lower prevalence (12.7%) than children of mothers with no history of measles (27.0%). Likewise, MV infection was significantly associated with maternal vaccine status ( $P=0.049$ ). Children of vaccinated mothers had a lower prevalence (17.1%) than children of unvaccinated mothers (27.0%, Table 5).

Of 273 children with fever, 58 (21.2%) were positive for MV immunoglobulin M antibodies. There was a significant association between MV infection and all presenting symptoms, except for vomiting, which showed no significant association ( $P=0.053$ , Table 6). There was no significant association ( $P>0.05$ ) between MV infection and malaria, typhoid, or pneumonia, which are common childhood illnesses with measles-like symptoms (Table 7).

## Discussion

The prevalence of MV found in children aged 0–8 months in this study is in agreement with the prevalence of 7.0% reported for Akwa Ibom State in children younger than 9 months<sup>8</sup> and the prevalence of 6% reported in Maiduguri, Borno State.<sup>9</sup> A prevalence of 61.6% was obtained in children aged 9–23 months in this study. The cumulative prevalence obtained in this study was 21.2%, suggesting that measles is endemic in Kaduna State and probably in Nigeria as a whole.<sup>10</sup> This was also reflected in the comparative prevalence between the hospitals, which showed no significant difference. This early presentation of measles has been attributed to waning maternal antibodies, especially in the setting where immunity is from vaccination not natural infection.

The overall prevalence of 21.2% obtained in children aged 0–23 months is lower than the prevalence of 30.2% reported in Akwa Ibom State<sup>11</sup> and 32.2% among older children in Giwa,<sup>10</sup> but higher than the 15.6% reported in another study from Southwestern Nigeria.<sup>12</sup> The reason for the observed differences may be attributed to the seriousness and dedication of relevant authorities in ensuring better measles vaccine coverage in their region. Accelerated measles control activities, including improved routine immunization coverage, provision of a second dose of measles vaccine as part of supplementary vaccination activities in certain countries of the world, and case-based surveillance with laboratory

**Table 3** Seroprevalence of measles virus infection in children in relation to their vaccination and nutritional status

Factors	Examined (n)	Positive (n)	Prevalence (%)	P-value	OR	CI
Vaccination status						
No	223	53	23.8	0.031*	2.81	1.059–7.432
Yes	50	5	10.0			
Breastfeeding						
No	28	17	60.7	0.00**	7.69	3.36–17.62
Yes	245	41	16.7			

**Notes:** Vaccination status,  $\chi^2=4.828$ ,  $df=1$ , OR 2.806,  $P=0.031$ ; breastfeeding,  $\chi^2=29.048$ ,  $df=1$ , OR 7.69,  $P=0.000$ ; vitamin A intake,  $\chi^2=23.568$ ,  $df=1$ , OR 7.28,  $P=0.00$ . \*Significant association exists at  $P<0.05$ ; \*\*significant association exists at  $P<0.01$ .

**Abbreviations:** CI, confidence interval; OR, odds ratio.

**Table 4** Seroprevalence of measles virus infection in children in relation to family type and possible risk factors

Factor	Examined (n)	Positive (n)	Prevalence (%)	P-value	OR	CI
Family type						
Polygamous	98	22	22.4	0.716	1.118	0.614–2.036
Monogamous	175	36	20.6			
Type of residence						
Self-contained	117	25	21.4	0.966	1.013	0.564–1.819
Shared apartment	156	33	21.2			
Household number						
>5	187	40	21.4	0.931	1.028	0.550–1.923
2–5	86	18	20.9			

**Notes:** Family type,  $\chi^2=0.132$ ,  $df=1$ , OR 1.118,  $P=0.716$ ; type of residence,  $\chi^2=0.002$ ,  $df=1$ , OR 1.013,  $P=0.966$ ; household number,  $\chi^2=0.007$ ,  $df=1$ , OR 1.028,  $P=0.931$ .

**Abbreviations:** CI, confidence interval; OR, odds ratio.

confirmation may have reduced measles-associated morbidity and mortality.<sup>13</sup>

In this study, females were seen to be more susceptible to measles infection than their male counterparts. This result is in agreement with previous studies in other parts of Nigeria<sup>11</sup> and Bolivia,<sup>14</sup> which documented that measles antibody is marginally higher in females than in males, but disagrees with the work of Chechet et al,<sup>10</sup> who reported the contrary. This finding showed that female children had two times higher odds of being infected with MV than their male counterparts.<sup>15–17</sup>

The test of association between parental level of education and the seroprevalence of measles showed no significant association. This finding disagrees with findings in Malawi<sup>18</sup> and Bolivia,<sup>14</sup> where seroprevalence was higher in children of mothers with less than a secondary education level, but lower in children of highly educated parents. The reason for this could be that infection with the virus remains endemic in Nigeria; as such, all the populace is equally exposed to it irrespective of their educational status.

There was no significant association between parental occupation and MV infection, contrary to the finding of Holmes et al,<sup>19</sup> where children of working class parents were more susceptible to infection. There was also no

significant association between number of children in the family and the prevalence of MV infection in this study.

The vaccination status of children was significantly associated with the prevalence of measles infection. Measles prevalence was higher in unvaccinated children (23.8%) than in children who were vaccinated (10%). The low level recorded for vaccinated children may reflect vaccine failure as well as effectiveness of vaccination. This study conforms to an acceptable measles vaccination threshold of >90%<sup>10</sup> as well as in early indication of failure stipulated in the range of 2%–10% reported by Wilkins and Wehle.<sup>20</sup> Problems with storage, transport, and maintenance of a cold chain system can easily affect the potency of vaccines in developing nations.<sup>12,21</sup> Diversification in measles strains has also been reported to account for the early presentation of measles and occurrence of measles in vaccinated children.<sup>22</sup>

The prevalence of MV was higher in children who were not breast feeding, compared with breastfeeding children, and non-breastfeeding children were at a 7.69 higher risk of being infected with MV than breastfeeding children. The low prevalence among breastfeeding children may be the result of a high level of antibodies and antimicrobials, as well as some probiotics contained in breast milk that confer immunity in these children. This study is in agreement with

**Table 5** Seroprevalence of measles virus infection in children in relation to maternal measles history and vaccination status

Factors	Examined (n)	Positive (n)	Prevalence (%)	P-value	OR	CI
Measles history						
No	163	44	27.0	0.005*	2.535	1.312–4.900
Yes	110	14	12.7			
Vaccination status						
No	115	31	27.0	0.049*	1.791	0.998–3.211
Yes	158	27	17.1			

**Notes:** Measles history,  $\chi^2=7.989$ ,  $df=1$ , OR 2.535,  $P=0.005$ ; vaccination status,  $\chi^2=3.873$ ,  $df=1$ , OR 1.791,  $P=0.04$ . \*Significant association exists at  $P<0.05$ .

**Abbreviations:** CI, confidence interval; OR, odds ratio.



**Table 6** Seroprevalence of measles virus infection in children in relation to disease symptoms

Factors	Examined	Positive (n)	Prevalence (%)	P-value	OR	CI	Factors
Fever	Yes	273	58	21.2	0.00*	Undefined	Undefined
	No	0	0	0.0			
Cough	Yes	127	34	26.8	0.037*	1.858	1.032–3.346
	No	146	24	16.4			
Coryza	Yes	7	24	32.0	0.008*	2.270	1.234–4.177
	No	198	34	17.2			
Diarrhea	Yes	182	46	25.3	0.021*	2.227	1.113–4.454
	No	91	12	13.2			
Vomiting	Yes	153	39	25.5	0.053	1.819	0.988–3.348
	No	120	19	15.8			
Rash	Yes	66	31	47.0	0.00*	5.905	3.14–11.09
	No	207	27	13.0			
Conjunctiva	Yes	14	7	50.0	0.007*	4.078	1.37–12.15
	No	259	51	19.7			
Koplik spots	Yes	4	3	75.0	0.008*	11.67	1.19–114.41
	No	269	55	20.4			

**Note:** \*Significant association exists at  $P < 0.05$ .

**Abbreviations:** CI, confidence interval; OR, odds ratio.

previous studies<sup>23,24</sup> showing that breastfeeding children are more resistant to measles infection.

Large family size and crowding in the home have been associated with the incidence of measles<sup>14</sup> but this was not established in our study. Similarly, no association was found between measles infection and type of residence or type of family, in contrast with the work of Burstrom et al,<sup>25</sup> and number of individuals in the household was established in this study in agreement with previous study carried out in the USA where there was no significant relationship between crowding and measles infection,<sup>26</sup> but in contrast with a study carried out in Bangladesh.<sup>27</sup>

This study established a relationship between maternal measles history and vaccination status with regard to the prevalence of measles in children. Children of mothers with no measles history had a higher prevalence than children of mothers with a measles history. This low observed prevalence in children of mothers with a measles history can be explained by the fact that these mothers have naturally acquired immunity against measles, which provides passive protection to

their infants. This agrees with previous studies by Brugha et al<sup>28</sup> and Nicoara et al.<sup>29</sup> Likewise, children of unvaccinated mothers had a higher prevalence and were at 1.8 times higher risk of being infected than children of vaccinated mothers. This could also be the result of vaccine-induced maternal immunity conferred to the children.<sup>28,29</sup>

This study established that all symptoms (fever, cough, coryza, diarrhea, rash, conjunctiva, and Koplik spots) had a significant association with MV. This means that a child with MV must present with some or all of these symptoms, and agrees with the work of Chechet et al,<sup>10</sup> it also agrees with the WHO clinical case definition, ie, any person presenting with a history of fever ( $39^{\circ}\text{C}$ – $41^{\circ}\text{C}$ ) lasting 3 days or more and generalized maculopapular rash with one of the following: coryza, cough, or conjunctivitis.<sup>30</sup>

There was no significant association between MV infection and other common childhood illnesses with measles-like symptoms. Although these illnesses present symptoms similar to those of measles, they may not necessarily be present in a child with MV infection.

**Table 7** Seroprevalence of measles virus infection in children in relation to common childhood diseases with measles-like symptoms

Factors	Examined (n)	Positive (n)	Prevalence (%)	P-value	OR	CI	Factors
Malaria	Yes	45	9	20.0	0.823	0.913	0.412–2.024
	No	228	49				
Typhoid	Yes	14	0	0.0	0.056	Undefined	Undefined
	No	259	58	22.4			
Pneumonia	Yes	4	0	0.0	0.295	Undefined	Undefined
	No	269	58	21.6			

**Notes:** Malaria,  $\chi^2=0.050$ ,  $df=1$ , OR 0.913,  $P=0.823$ ; typhoid,  $\chi^2=3.981$ ,  $df=1$ ,  $P=0.056$ ; pneumonia,  $\chi^2=1.095$ ,  $df=1$ ,  $P=0.295$ .

**Abbreviations:** CI, confidence interval; OR, odds ratio.

## Conclusion

The findings of this study confirm the presence of MV in children aged 0–8 months in Kaduna State, with a seroprevalence comparable with rates obtained in other parts of the country. The prevalence of 6.5% obtained in children aged 0–8 months and 21.2% in children aged 0–23 months is an indication that measles is endemic in Kaduna State and still poses a public health problem, despite the availability of a safe and effective vaccine. Therefore, it is important for health providers and policy makers to recognize the health implications of this virus, review the vaccination age of infants, and intensify vaccination campaign programs. This study recognized age, sex, vaccination, breastfeeding, vitamin A intake, and maternal vaccination and measles history as important demographic risk factors for MV infection in children.

## Disclosure

The authors report no conflicts of interest in this work.

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