ORIGINAL ARTICLE

Measles Immunoglobulin G Levels Amongst Under Fives in a Northeastern State of Nigeria

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ABSTRACT

Background: Measles is the most prevalent and leading cause of death among vaccine-preventable diseases. Nigeria has one of the highest burdens of measles worldwide and this burden can be reduced significantly with development of protective antibodies through vaccination. **Objective:** This study assessed the measles immunoglobulin G levels amongst children aged one to five years. **Methods:** a cross-sectional study design was used to study 229 children seen at the Paediatric General Outpatient Department of the University of Maiduguri Teaching Hospital, Maiduguri using a structured questionnaire. Blood samples were collected for estimation of measles immunoglobulin levels. Data was entered into and analysed using the Statistical Package for Social Sciences (SPSS) Version 20.0 (IBM SPSS, 20.0). **Results:** Of the 229 children studied, 145 (63.3%) had measles vaccination while 202 (88.2%) had protective measles antibody levels. The proportion of protective antibodies was significantly more amongst the vaccinated children than the unvaccinated children (135, 93.1% Vs 67, 79.8%; $\chi 2 = 22.88$, $P < 0.0001$). Similarly, amongst those with a high antibody titre of >220 mIU/ mL, 133 (67.5%) had measles vaccine while 64 (32.5%) were unvaccinated ($\chi 2 = 10.836$, $P = 0.013$). **Conclusion:** Despite the low immunisation coverage observed in this study, most children demonstrated protective antibody titres, with vaccinated children having significantly higher antibody titres compared with unvaccinated children.

Key words: Measles, immunoglobulin G, protective antibodies, vaccination, under-5 children.

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Introduction

Measles is a highly contagious vaccine-preventable disease (VPD) caused by a morbillivirus often occurring in epidemics. The illness is characterised by high fever, and the appearance of maculopapular rashes with one or more of the following: coryza, conjunctivitis, cough and Koplik spots. It is associated with high mortality mainly from complications like pneumonia, diarrhoea, and malnutrition.[1,2]

Globally, VPDs account for about two million deaths yearly with 1.5 million occurring in children less than five years of age, constituting 15% of under-five deaths.[3] In Nigeria, VPDs account for 22% and 17% of under-five (U5) morbidity and mortality respectively.[4] Measles has been reported to be the most prevalent and the leading cause of death among VPDs in children.[5,6]

Efforts to reduce the global burden of measles have been made since the discovery of the safe and effective measles vaccine in 1963 to date. Vaccination against measles has led to a reduction in the case burden by a 75% drop in mortalities between 2000 and 2013.[7]

Despite global progress, measles control remains a challenge in sub-Saharan Africa as Nigeria is still one of the 47 priority countries in the world where the burden of the disease is highest with outbreaks reported in various states.[7,8]

In Nigeria, the measles vaccine is currently administered at 9 months and 15 months of age under the National Programme on Immunization (NPI). World Health Organization and United Nations International Children's Emergency Fund (UNICEF) estimated Measles Containing Vaccine (MCV) coverage in Nigeria at 33% in 2000, and 44% in 2006 and remained at 41% between 2007 and 2008. However, the coverage reported by WHO and UNICEF was 38% in 2005, 86% in 2007 and 68% in 2008.[9] By 2011, 1.7 million Nigerian children had not received the first dose of measles vaccine[10] and 843 cases of measles were reported in the same year. In 2013, another outbreak was reported with 29,000 cases in some states in northern Nigeria.[8] Measles Containing Vaccine (MCV1) coverage as of 2016/ 2017 in Nigeria was 42% according to the National Immunization Coverage Survey (NICS),[11] however, a coverage of 51% was reported by the Nigeria Demographic and Health Survey (NDHS) 2024. As of August 2019, Nigeria had reported 30,457 suspected cases to the WHO of which 24,994 were confirmed.[12]

Measles antibodies develop in approximately 95% of children vaccinated at 12 months of age and 98% of children vaccinated at 15 months of age.[13,14-16] It is estimated that 2-5% of children who receive the vaccine at 12 months of age or younger or who only get a single dose of measles-containing vaccine fail to be protected.[16] Although the titre of vaccine-induced antibodies is lower than that following natural disease, both serologic and epidemiologic evidence indicate that vaccine-induced immunity appears to be long-term and probably lifelong in most persons.[16,17] Most vaccinated persons who appear to lose antibodies show an anamnestic immune response upon revaccination, indicating that they are probably still immune.[16]

The protective level of measles neutralizing antibody is estimated to be 200 mIU/mL based on the First International Reference serum, 120 mIU/mL based on the Second International Reference serum and recently, > 120 mIU/mL based on the 3rd International Standard Reference serum.[18]

In a study by Hamid *et al* [19] in Kano, Nigeria protective levels of measles antibodies were found in 65.6% of the children aged less than 10 years. Similarly. Opaleye OO *et al*[20] in South-Western Nigeria studied the prevalence of measles-neutralizing antibody titres in children less than 15 years where 89.5% had detectable neutralizing antibodies but only 57.9% had protective antibody titres. Onoja *et al*,[21] also reported that 66.8% of the children studied in Kano had protective levels of antibodies while 73% of those studied in Ibadan were protected. A study of 138 children aged 0-36 months in Lagos by Oyefolu *et al*[22] reported that 55.1% of all the studied subjects were seropositive for measles antibodies. However, of those aged ≥ 12months, 70.5% had detectable levels of antibody out of which 77.4% of them had protective levels suggesting a high seroconversion rate.

This study assessed the measles Immunoglobulin G (IgG) levels in children aged 1-5 years seen at the University of Maiduguri Teaching Hospital (UMTH), Maiduguri, Borno State, Nigeria.

Methods

Study area

The study was carried out at the Paediatric General Outpatient Department (GOPD) of UMTH, Borno State, Nigeria. The UMTH is a centre of excellence for infectious diseases and immunology.

Study design

It was hospital-based, descriptive cross-sectional study.

Study Population

The study population was children aged one to five years attending the Paediatric GOPD, UMTH. Children less than one year were not included due to possible interference of maternally acquired antibodies as well as insufficient doses of measles vaccine as the recommended age for MCV2 is 15 months.

Sample Size Determination

The statistical formula, $n = \frac{z^2pq}{d^2}$ was used, where:

n = The minimum sample size when the population is more than 10,000.

Z = Standard normal deviation, usually set at 1.96 corresponding to a 95% confidence interval.

P = 0.82 = expected proportion of children with protective levels of anti- measles IgG, extrapolated from the study finding in Kano, Northwest Nigeria[23] where 81.6% of children were found to have protective levels of anti-measles IgG.

P = 0.82

q = 1.0 – 0.82 = 0.18

d = level of precision = 0.05 (5%).

Therefore, the minimum sample size (n) = $\frac{(1.96)^2 (0.82)(0.18)}{(0.05)^2}$

n = 236.

Using the statistical formula[102] $nf = \frac{n}{1+\frac{n}{N}}$ for population less than 10,000, where:

c= the desired sample size when the population is less than 10,000.

n = the desired sample size when the population is more than 10,000 (already calculated as 236).

N = the estimate of the population size. The average annual population of children ≤ 5 years seen at POPD UMTH is 6,871.

A sample size (nf) was calculated as 228.

An attrition of 10% was added to take care of logistics and misplaced samples making the total sample size to be = 251.

Total Sample Size = 251.

Inclusion criteria

1. Children who presented to the POPD for follow up or with minor illnesses
2. Children aged one to five years.
3. Parental or guardian consent to the study.

Exclusion criteria

1. Children with history of administration of measles immune globulin, blood transfusion, measles vaccination in the preceding 4 weeks and
2. Children with active measles infection.

The children were selected using systematic random sampling.

Ethical Consideration

The study protocol was reviewed and approved by the Ethical Review Committee of the UMTH. The research aims and procedures were duly explained to each parent/ caregiver. Signed or thumb-printed informed consent was obtained from each parent/ caregiver.

Data Collection Procedures

A structured questionnaire was administered to obtain used to obtain information on socio-demographic variables (age, sex and social class), history of vaccination against measles and for unvaccinated subjects, reasons for not receiving the vaccine. Parents of unvaccinated children were counselled. Social class was determined using Oyedeji Social Classification scheme.

Sample collection

Two millilitres of venous blood were obtained from a peripheral vein following a standard aseptic procedure. The samples were then centrifuged within two hours of collection and separated at the Immunology Laboratory. Aliquots of serum samples were then stored at -20 ^{0}C until analysis. All samples were assayed for measles immunoglobulin G (IgG) antibodies.

Measles IgG Estimation

This was done using a qualitative and semi-quantitative ELISA test kit (Demeditec Measles Virus IgG ELISA DEMEAG0330). The assay was carried out according to the user's manual.

Calculation of Results

The optical densities of the specimens as well as controls were used to calculate results in standard units as per the assay protocol.

$$\text{Units} = \frac{\text{Sample absorbance value x 10}}{\text{Cut off}}$$

The standard units had their equivalents of antibodies in mIU/ mL from the manufacturers based on the WHO 3rd international reference standard serum. Protective measles antibody level has recently been put at > 120 mIU/ mL based on the 3rd International Standard Reference serum.[14,24] For this study, an antibody level of >120 mIU/ mL was used as the cut-off value below which the subject was classified as not protected.

Data Analysis

Analysis was done using the Statistical Package for Social Sciences (SPSS) Version 20.0 (IBM SPSS, 20.0). Numerical variables such as the age of subjects were summarized using mean and standard deviation. Categorical variables were expressed as frequencies and proportions, and Chi-squared or Fisher's Exact test was used to analyse for difference as appropriate. Tables and Figures were used to present the findings. A p-value of less than 0.05 was considered significant at a 95% confidence interval.

Results

This study assessed the measles Immunoglobulin G levels in children aged 1-5 years seen at the UMTH

from November 2020 to December 2021. Of the 251 samples collected from 251 subjects, 19 got misplaced at the Laboratory during the upgrading and renovation of the Laboratory to a Molecular laboratory for COVID-19 PCR. Three (3) samples were not suitable for analysis due to haemolysis. Thus, 229 (91.2%) subjects had their samples processed and data analysed.

Table I shows the sociodemographic characteristics of the study population. Subjects aged one year at their last birthdays constituted the majority, 90 (39.3%). There were 126 (55%) males and 103 (45%) females giving a male-to-female ratio of 1.2: 1. Most of the subjects belonged to social classes III and IV with frequencies of 69(30.1%) and 61 (26.6%) respectively.

Table I: Sociodemographic Characteristics of Subjects.

	Frequency (N = 229)	**Percentage (%)**
Characteristics		
Age (Years)		
1	90	39
2	78	34
3	32	14
4	18	8
5	11	5
Sex		
Male	126	55.0
Female	103	45.0
Social Class		
I	20	9
II	46	20
III	69	30
IV	61	27
V	33	14

Measles Immunisation Coverage

One hundred and forty-five out of the 229 subjects eventually studied had received the measles vaccine giving a measles vaccination coverage of 63.3% among the subjects.

Reasons For Lack of Vaccination.

Eighty-four out of the 229 subjects studied were unvaccinated. The most frequent reasons for lack of vaccination were ignorance 33 (37.5%) and negligence 32 (36.4%), others include lack of access to immunisation facilities, adverse events with other vaccines and parental refusal. (Table II).

Table II: Reasons for Lack of Vaccination.

Reasons	Frequency (N=84)	Percentage (%)
Ignorance	33	37.5
Negligence	32	36.4
Lack of geographic access	8	9.2
Adverse events with other vaccines	4	4.5
Active measles infection	1	1.1
Frequent ill health	1	1.1
Parental refusal	3	3.4
Others	6	6.8
Total	**88**	**100**

NB: Some had multiple responses.

Proportion Of Children with Measles Protective Igg Antibody Levels.

Overall, 202 (88.2%) subjects had protective measles antibody levels. Those vaccinated were significantly more protected (93.1%) than their unvaccinated counterparts (79.8%). ($\chi^2 = 9.11$, P = 0.003).

Vaccination status	Protective Antibodies	No protective Antibodies	Total	χ^2	P-value
Vaccinated	135	10	145	9.11	0.003
Unvaccinated	67	17	84		
Total	**202**	**27**	**229**		

Measles Infection Amongst Vaccinated and Unvaccinated Subjects.

Table III shows that unvaccinated subjects were more likely to have had a history of measles infection compared to their vaccinated counterparts ($\chi^2 = 9.51$, P = 0.002).

Table III: Measles Infection Amongst Vaccinated and Unvaccinated Subjects. (N=229)

Measle infection	Vaccinated N=145	Unvaccinated N=84	Total	χ^2	P – value
Yes	19 (13.1%)	25 (29.8%)	44	9.51	0.002
No	126 (86.9%)	59 (70.2%)			
Total	**145 (100%)**	**84 (100%)**			

Measles IgG Antibody Levels In Vaccinated and Unvaccinated Subjects.
Table IV shows the comparison of antibody levels in vaccinated and unvaccinated subjects. Overall, most of the subjects (vaccinated and unvaccinated) had a high antibody titre of >220mIU/ mL. However, those vaccinated were significantly more likely to have a high antibody titre of >220 mIU/ mL (χ^2 = 10.836, P = 0.013).

Table IV: Antibody Levels in Vaccinated and Unvaccinated Subjects

Antibody (mIU/ml) titre	Frequency (%) Vaccinated (N=145)	Unvaccinated (N=84)	Total	Chi-squared (χ^2) Test	P-Value
≤ 120	10 (37.0)	17 (63.0)	27	10.836	**0.013**
> 120 – 170	1 (33.3)	2 (66.7)	3		
> 170 – 220	1 (50.0)	1 (50.0)	2		
> 220	133 (67.5)	64 (32.5)	197		

Vaccinated subjects had significantly more protective antibody levels compared to unvaccinated subjects (135, [93%] versus 67, [79.8%]; χ^2 = 9.103; P- value = 0.003) as shown in Figure 1.

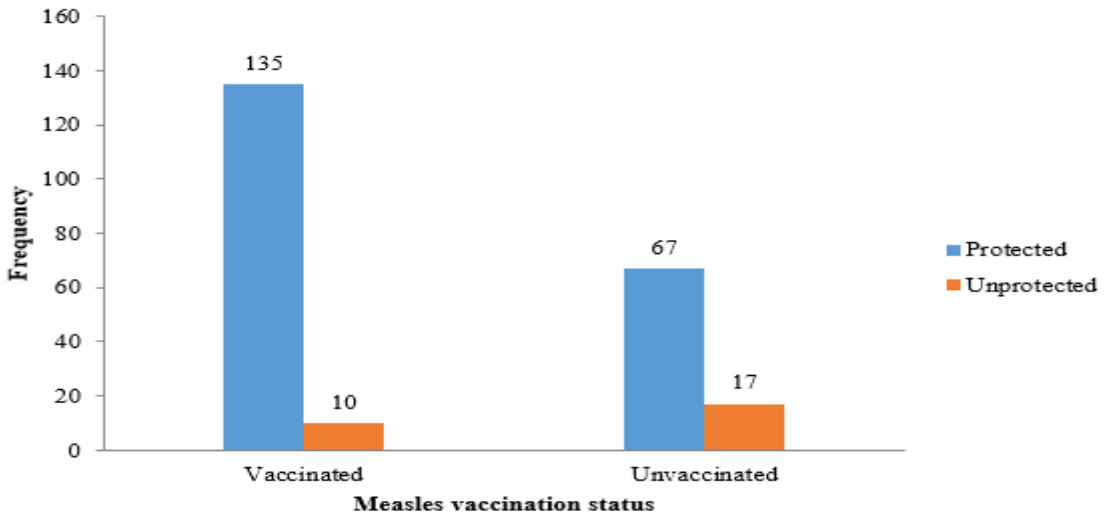

Figure 1: Measles Immunoglobulin G Antibody Levels Amongst Vaccinated and Unvaccinated Subjects

Discussion

From this study, the measles vaccination coverage was high (63.3%), signifying some improvement in the immunisation activities in the state. This is higher than the 58.1% and 46% reported by the National Immunisation Coverage Survey (NICS2016) and National Demographic Health Survey (NDHS2018) for Borno State.[11,12] The higher rate observed, could be explained by the fact that the study was hospital-based, within the state Capital where access to health care services is good and the subjects recruited presented to the Paediatric GOPD with mild-moderate illnesses. Also, parents presenting to the tertiary facility to seek healthcare generally could be assumed to have a good attitude towards the preventive aspect of health such as immunisation services as seen in the present study. The vaccination higher rate could also reflect the outbreak response immunisation following the measles outbreak in the state in 2019 with a post-campaign coverage of 85%.[25] The coverage from this study is, however, lower than reports from Kano (66.4%),[26] Ibadan (70%),[26] and Bangui, Central African Republic (83.1%).[27] This may be explained by a smaller sample size of 251 and the limited age range of 1-5 years used in this study. This finding calls for further improvement in the immunisation activities within the study area to reach the WHO target to attain herd immunity.

The study revealed that most of the subjects (88.2%) had protective levels of measles antibodies (> 120 mIU/mL) suggesting a high level of protection against measles infection. This finding is higher than 77.4% in Lagos,[22] 65.6 % in Kano[19], 57.9% in South Western Nigeria,[20] 47.8% in Zaria[28] and 29.2% in Abuja.[29] The finding is however lower than the 95% recommended by WHO[30] and 89.5%, 98.2%, 87.7% and 91.13% reported in Germany, United Arab Emirates, Italy, and China, respectively.[29,31-33] The high proportion of subjects having protective levels of antibodies from this study can be explained by the high vaccination rate of 63.3% among the subjects since the measles vaccine is safe, effective and known to induce long-term and probably lifelong immunity.[13,16] Natural measles infection is another source of protective antibody levels however, in this study, only 19.2 % of subjects had measles infection and this was not significantly associated with protective antibody levels amongst both vaccinated and unvaccinated subjects. Subjects in this study that were vaccinated were significantly more protected than their unvaccinated counterparts. This finding is similar to reports from the Central African Republic.[25]

Knowledge of the reasons for subjects not receiving the vaccine is very important to aid improvement in policies and institute targeted interventions to improve the uptake of vaccines. From this study, the major reasons for non-vaccination are ignorance (37.5%) and negligence (36.4%). This is not unconnected with the fact that most of the subjects are from middle-lower social classes with primary or no education at all which is linked to ignorance and poor health-seeking behaviour.

Conclusion

Measles vaccination coverage in this study is low. Most of the children studied had protective levels of measles Immunoglobulin G antibodies. Significantly more of the vaccinated children had higher protective levels of measles Immunoglobulin G antibodies compared to their unvaccinated counterparts.

Recommendations

There is a need for improvement in the measles immunisation coverage to meet the WHO target of $\geq$ 95% required to achieve herd immunity. Parents should be encouraged to vaccinate their children against measles through the provision of education to the parents and access to healthcare facilities in Nigeria.

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