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**Re-occurring cases of under-five Measles infection in North-Western Nigeria-the need to increase immunization coverage.***Basirka, N.L.<sup>1\*</sup>, Sarkinfada, F.<sup>2</sup>, Gadama, A.S.<sup>3</sup>, Mohammed, Y.<sup>4</sup>, Abubakar, M.U.<sup>5</sup>**Gwaram Cottage Hospital, Ministry of Health, Jigawa State, Nigeria<sup>1</sup>, Department of Health and Medical Sciences, Khawarizmi International College Abu Dhabi, UAE<sup>2</sup>, General Hospital Ningi, Hospital Management Board, Bauchi State, Nigeria<sup>3</sup>, Department of Medical Microbiology and Parasitology, College of Health Sciences, Bayero University Kano, Nigeria<sup>4</sup>, Yadakunya Hospital, Hospital Management Board, Kano State, Nigeria<sup>5</sup>.**Author for Correspondence\*:nlawalb@gmail.com / +234-806-926-7676***Abstract**

Measles infection is caused by a highly contagious measles virus (MV). MV is the leading cause of vaccine preventable death among under-five children globally. The widespread adoption of the measles vaccine in national immunization programmes since the establishment of the expanded programme on immunization (EPI) in Nigeria, has marked a decrease in the number of reported cases. But the pre-vaccine era trend is gradually returning owing to poor attitude of the populace on immunization. The aim of the study was to assess the seroprevalence of measles antibodies among under-five measles infected children in Gwaram Cottage Hospital, Jigawa State, Nigeria. The study was a cross-sectional study involving measles infected under-fives as the study subjects. Sociodemographic characteristics were obtained using a semi-structured questionnaire and five milliliters of blood samples were collected and processed to obtain serum. Serum was used to test for Measles specific IgM and IgG antibodies using Enzyme-linked immunosorbent assay (ELISA). Of the 91 study subjects analyzed, 63(69.2%) had at least IgM and IgG antibodies. A total 17(18.7%) had isolated IgM while 16 (17.6%) had isolated IgG. A total 30 (32.9%) of the study subject has both IgM and IgG concurrently. No statistically significant association was found between measles specific IgM and IgG with most of the sociodemographic factors except for measles specific IgG and immunization history ( $p=0.001$ ). The study has shown high prevalence of Measles antibodies among the study subjects with poor level of immunization, making the

study area at risk of measles infection especially among under-fives and immunocompromised children and adults, hence, the need to intensify immunization against measles virus.

**Keywords:** measles infection, under-fives, seroprevalence, immunization

**Introduction**

Measles virus (MV) belongs to the family Paramyxoviridae, the genus Morbillivirus and the order Mononegavirales. It is the causative agent of the childhood deadly disease; measles infection (Griffins and Bellini, 1996). MV was first isolated by John Enders and Thomas Peebles in the 1950s from the blood sample of a measles infected person (Rima and Duprex, 2006; Enders and Peebles, 1954). It is a single stranded RNA, non-segmented, enveloped virus with helical symmetry (Griffin, 2001).

Measles is the leading cause of vaccine-preventable death among children under 5 years globally (WHO, 2011). In the 1980s, the measles virus killed an estimated 2.6 million children each year worldwide (WHO, 2011). In the years 2000 to 2011 however, the number of measles cases reported worldwide began to decrease significantly by 58% (from 853,480 to 354,922) and measles incidence decreased by 65% (from 146 to 52 cases per million population per year) (WHO, 2011) In 2008 the number of cases reported worldwide reached as low as 278,417. From 2010, the global pattern of yearly measles cases reports began to increase each year and large outbreaks of measles have been reported in several countries (CDC, 2013). In 2011 there

were 327,305 cases reported with approximately 158 000 global deaths from measles predominantly among children under the age of five years (Simons *et al.*, 2012). Despite the availability of a safe and effective vaccine for over forty years, Measles remains the leading cause of vaccine-preventable childhood mortality globally (Liu *et al.*, 2012).

Nigeria is still one of the 47 priority countries in the world where the burden of the disease is highest with outbreaks of measles still being reported in various states. Reports in 2011 revealed that about 1.7 million Nigerian children are yet to receive the first dose of the Measles Conjugate Vaccine and a total of 18,843 cases of measles was reported (WHO 2012). In 2013 also, measles outbreak occurred with 29,000 cases of measles reported in some states in Northern Nigeria.

Presently, the global Measles and Rubella Strategic Plan 2012-2020 has been developed with a five-pronged strategy to cut global measles deaths by at least 95% by 2015 compared with the 2000 levels and to achieve measles and rubella elimination in at least 5 of the 6 World Health Organization regions by 2020 (WHO 2012). Nigeria been part of the WHO region of Africa is yet to incorporate the combined Measles and Rubella (MR) vaccine into its routine immunization schedule, although it has been endorsed by the Pediatrics Association of Nigeria (PAN Advisory Committee of Immunization, 2012).

A recent study reported an immunization coverage of 6.5% among under 5 year's children in a semi-nomadic community of Kano, with only 30% of under-fives receiving at least one form of immunization in the last one year. Majority of the populace including caregivers (70.2%) indicated that they do not consider immunizing their children necessary (Musa *et al.*, 2016).

### **Materials and Methods**

The study was carried out in Gwaram Cottage Hospital of Gwaram Local Government Area of Jigawa State, Nigeria. The study includes under five years of age children with clinical diagnosis

of active measles infection admitted in Gwaram Cottage Hospital. The following diagnostic criteria was used in selecting the study subjects.

### **Inclusion Criteria**

- High grade fever preceding the appearance of the rash by about 2-4 days
- A generalized erythematous maculo-papular non-vesicular rash
- One or more of the following: cough, conjunctivitis or coryza

### **Exclusion Criteria**

Patients suspected or known to have Sickle cell disease, HIV/AIDS, Autoimmune diseases, leukemias and other similar illnesses known to mimic measles infection were excluded from the study through history taking. A cross-sectional study was used. Ninety-one (91) measles infected Under-five years of age children were selected using convenient sampling method.

### **Ethical Approval**

Ethical approval was obtained from the ethical committee of Jigawa State Ministry of Health and a letter of ethical approval notification was issued to the management of Gwaram Cottage Hospital prior to the commencement of the study.

### **Informed Consent**

Verbal informed consent was obtained from each subject through their care-givers using informed consent form. Adequate explanation on the nature and relevance of the study was communicated to the care-givers prior to signing the form. Those that wish not to participate were excluded.

### **Sample collection**

A qualitative data on demographic characteristics of the participants was obtained using a semi-structured interviewer questionnaire through their informants/care-givers. Five milliliters (5ml) of venous blood sample was equally collected from each subject following strict aseptic procedure.

### **Sample Analysis**

Blood samples collected from each subject was processed to obtain serum. Serum samples were

analysed to quantitatively detect the presence of Measles-specific IgM and/or IgG antibodies using enzyme linked immunosorbent assay (ELISA).

**Statistical Data Analysis**

Data obtained were analyzed using Microsoft and SPSS software version 20 (2011, IBM Corporation, U.S.A.). Sociodemographic data was summarized in tables and presented in percentages. Chi square test was used to test for association between demographic factors Measles-specific IgM/IgG antibodies. A p-value of  $\leq 0.05$  considered significant.

**Results**

**Sociodemographic characteristic of Measles Infected Children.**

Ninety-one Measles infected children were studied and constituted the study group (Table 1). Majority of the study subjects (38.5%) are between the ages of 13 to 24 months with mean age of 2.30 months and SD 0.983. Majority of the subjects were females (50.5%). Past history of measles Immunization was present in 6 (20.9%) of the measles infected children, while the majority (93.4%) had no history of measles immunization at all (Table 4.1).

**Table 1. Sociodemographic characteristic of Measles Infected Children (N=91)**

Characteristics	Number	Percentage
<b>Age (Months)</b>		
1-12	21	23.1
13-24	35	38.5
25-36	22	24.2
37-48	13	14.2
<b>Gender</b>		
Male	45	49.5
Female	46	50.5
<b>Past Hx of Measles</b>		
Present	19	20.9
Absent	72	79.1
<b>Immunization Hx</b>		
Present	6	6.6
Absent	85	93.4

**Categories of Measles infection among the Study subjects**

Considering the distribution of Measles antibodies among the study subjects, 18.7% had early infection, 32.9% had recent infection, and 17.6% had developed immunity while 30.8% had no immunity (Table 2).

**Table 2: Categories of Measles Infection among the Study Group.**

Immune response	Frequency	Percentage (%)	Interpretation
IgM (+) IgG (-)	17	18.7	Early infection
IgM (+) IgG (+)	30	32.9	Current infection
IgM (-) IgG (+)	16	17.6	Immuned
IgM (-) IgG (-)	28	30.8	No immunity
Prevalence	63	69.2	Total prevalence

**Comparison between Sociodemographic Factors and Measles Specific IgM among the Study subjects.**

Comparism was made between Measles Specific IgM with age, gender, past history of measles infection and history of immunization (Table 3). No statistically significant association was found between Measles Specific IgM antibodies with either of the sociodemographic factors using p-value  $\leq$  0.05 as significant.

**Table 3: Comparison between Sociodemographic Factors and Measles Specific IgM among the study subjects.**

Characteristics	MV-specific IgM			p-value
	Positives	Negative	Total	
<b>Age (months)</b>				
1-12	8 (38.1%)	13 (61.9%)	21 (23.1%)	
13-24	20 (57.1%)	15 (42.9%)	35 (38.5%)	2.613
25-36	13 (59.1%)	9 (40.9%)	22 (24.2%)	
37-48	6 (46.2%)	7 (53.8%)	13 (14.3%)	
<b>Gender</b>				
Males	26 (57.8%)	19 (42.2%)	45 (49.5%)	1.339
Females	21 (45.7%)	25 (54.3%)	46 (50.5%)	
<b>Past hx of measles</b>				
Present	8 (42.1%)	11 (57.9%)	19 (20.9%)	0.876
Absent	39 (54.2%)	33 (45.8%)	72 (79.1%)	
<b>Immunization hx</b>				
Present	2 (33.3%)	4 (66.7%)	6 (6.6%)	0.863
<b>Absent</b>	45(52.9%)	40 (47.1%)	85 (93.4%)	

**Comparison between Sociodemographic factors and Measles Specific IgG among study subjects.** Comparism was made between Measles Specific IgG with age, gender, past history of measles infection and history of immunization (Table 4). There was a statistically significant association between immunization history and Measles Specific IgG. However, no significant association was demonstrated statistically between Measles Specific IgM antibodies with the other sociodemographic factors using p-value  $\leq 0.05$  as significant.

**Table 4: Comparison between Sociodemographic factors and Measles Specific IgG among study group.**

Characteristics	MV Specific IgG			p-value
	Positive	Negative	Total	
<b>Age(months)</b>				
1-12	8(38.1%)	13(61.9%)	21(23.1%)	2.153
13-24	20(57.1%)	15(42.9%)	35(38.5%)	
25-36	12(54.5%)	10(45.5%)	22(24.2%)	
37-48	6(46.2%)	7(53.8%)	13(14.3%)	
<b>Gender</b>				
Male	24(53.3%)	21(46.7%)	45(49.5%)	0.276
Female	22(47.8%)	24(52.2%)	46(50.5%)	
<b>Past Hx of Measles</b>				
Present	7(36.8%)	12(63.2%)	19(20.9%)	1.805
Absent	39(54.2%)	33(45.8%)	72(79.1%)	
<b>Immunization hx</b>				
Present	3(50.0%)	3(50.0%)	6(6.6%)	0.001
Absent	43(50.6%)	42(49.4%)	85(93.4%)	

**Discussion**

Measles is one the most common vaccine preventable disease which affects mostly children under five years of age (Musa *et al.*, 2016). Prevalence continue to rise over the years owing to poor vaccine seeking behavior that is often attributed to sociocultural attitudes and beliefs.

Findings of this study revealed that the seroprevalence of 63 (69.2%) for at least IgG and IgM were obtained among the study subjects, suggesting that subjects were exposed to measles virus from previous infection, vaccination or community exposure. A significant proportion (32.9%) of the study group had both IgM and IgG (IgG<sup>+</sup>, IgM<sup>+</sup>) demonstrating that the serological

index of current infection (IgM and IgG positive group) appears to be high. During the course of infection at about seven days following the appearance of the rash to about 35 days, both IgM and IgG can be assayed concurrently before finally IgM disappears. The result obtained in this study is in conformity with the study done in Kaduna State –Nigeria (Olaitan *et al.*,2015), which demonstrated a prevalence of 35.1% and 81.6% for measles IgM and IgG among children aged 1-5 years. The prevalence from the study is in contrast with a study from Bangui, Central Africa Republic which shows a prevalence of measles virus IgG (IgG<sup>+</sup>, IgM) of 57.3%, among children aged 9 months to 5years (Manirakiza *et al.*,2011).

While 18.7% was obtained for IgM alone (IgG<sup>-</sup>, IgM<sup>+</sup>) among subjects, almost equal percentage (17.6%) was obtained for IgG (IgG<sup>+</sup>, IgM<sup>-</sup>) alone. Result indicated that 32.9% was the prevalence obtained for both IgG and IgM (IgG<sup>+</sup>, IgM<sup>+</sup>) and 30.8% of the study subjects have neither antibody demonstrated serologically (IgG<sup>-</sup>, IgM<sup>-</sup>). The negative results for both IgG and IgM could be as a result of clinical misdiagnosis, concurrent immunosuppressive conditions, or sample were taken in the window period. In tropical environments, approximately one third of primary dengue virus infections can present with rash and fever accounting for the vast majority of rash and fever cases seen in dengue epidemic periods, this could lead to misdiagnosis and eventual negative results for both IgG and IgM (WHO, 2007).

Sub-group with isolated IgM forms the most important group since 90% of measles cases are confirmed via the IgM obtained by the use of sensitive ELISA (Tipple *et al.*, 2003).

Towards the end of infections at around 35 days following the appearance of rash, IgM usually disappears with the persistence of IgG to confer immunity for lifetime except otherwise conditions with defective cellular immunity like HIV/AIDS ensures in the future (Tipple *et al.*, 2003). These could explain the group of subjects with IgG alone (IgG<sup>+</sup>, IgM<sup>-</sup>).

Finding from this study indicates that 33.3% of the subjects that had history of immunization, yet

came up with symptoms suggestive of measles infection. It is worth stressing that recent MR or MMR vaccine recipients are likely to be represented among cases of rash-and-fever associated with other pathogens, and a vaccine-associated IgM response erroneously attributed to measles or rubella infection. Since immunization with Measles/Rubella (MR) or Measles/Mumps/Rubella (MMR) vaccine stimulates measles- and rubella-specific IgM responses, a history of MR or MMR vaccination within 6 weeks of rash onset makes the interpretation of serological results problematic (WHO,2007). Serological techniques cannot distinguish between the immune response to natural infection and immunization, this can only be accomplished by viral isolation and characterization (WHO, 2007)

It is therefore recommended that IgM-positive cases with a history of measles and/or rubella vaccination in the 1 to 6 weeks prior to rash onset can be discarded after thorough epidemiological investigation and no evidence is found of other confirmed cases in the vicinity or an epidemiological link to confirmed cases elsewhere. Vaccines that had lost their potency either through poor cold-chain maintenance or expiry, could also allow for the development of active measles (IgG<sup>+</sup>, IgM<sup>+</sup>). Therefore, this could be another view to the explanation.

A total of 66.79% of the remaining subjects though have no IgM, had immunization and yet developed symptoms suggestive of Measles infection. This could be as a result of misdiagnosis or rather had lost IgM with subsequent development of IgG.

Results from this study indicated that 50% of the subjects had IgG (IgG<sup>+</sup>, IgM<sup>-</sup>) among the subject that had immunization, yet presents with symptoms suggestive of measles infection. This could be that the subjects had lost IgM with development of IgG or were recovering from post immunisation manifestations. 50% of the subjects had immunisation yet do not have IgG in their serum, signifying either a misdiagnosis or had received faulty vaccines.

No association was found between

sociodemographic factors and Measles-specific IgM/IgG except between measles-specific IgG and Immunization history ( $p= 0.001$ ) with majority of the cases falling in the unimmunized group. This is anticipated in a place where the immunization coverage is poor evidenced by the fact that only 6.6% of the study subjects were immunized.

### Conclusion

The study has demonstrated a high prevalence of Measles-specific IgM and IgG antibodies with a dominant proportion of children unimmunized. Thus, putting the whole population at risk of measles infection. The high prevalence also points that children and adults exposed to conditions of Immunosuppression like HIV/AIDS would suffer the consequence of primary infection and reinfection. A significant number of the subject developed clinical symptoms indicative of measles infection despite been immunized, which could be attributed to vaccine induced immune response or measles virus in situation of poor potency or expired vaccine.

### Recommendation

1. There is need to improve the means through which information on measles vaccine is delivered to the public so that all children will get vaccinated.
2. There is need for strengthening policy on immunization against child killer disease including measles in order to reduce the under-fives mortality to the minimum.
3. There is need to strengthen vaccine cold-chain maintenance and other vaccine management measures in order for the vaccines to remain potent.

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