Incidence of measles specific IgG antibody among children in Adamawa State, Nigeria

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Abstract

Measles account for nearly half of the 1.7 million annual deaths due to childhood vaccine-preventable diseases. Presence of measles specific IgG antibodies has been proven to correlate with protection (immunity) to natural measles infection. This study was therefore designed to determine the prevalence of measles specific IgG antibody and also to determine the association between prevalence of measles specific IgG antibody and age, gender, as well as history of measles infection among children aged 0-14 years in Adamawa State. The research was carried out within the three senatorial districts of the State. Serum samples (368) collected from children were used to determine the prevalence using ELISA method. Questionnaire was used to obtain demographic data of the children relevant to the study. The study revealed that 227 (61.6%) of the children had protective measles IgG antibody with antibody titre ranging from 10-250 U/mL, while 141 (38.4%) had non-protective measles IgG antibody. There was significant association between history of measles infection and protective antibodies (P-value =0.000), but there was no significant association between gender (P-value = 0.958), age (P-value = 0.140) and protective measles IgG antibody.

Keywords: IgG antibody, Immunity, Measles virus, Vaccination.

INTRODUCTION

Measles is a highly contagious viral disease and a major cause of morbidity and mortality among children worldwide and especially in Africa and Southern Asia (Mossong and Muller, 2003; World Health Organisation [WHO], 2001). The disease is caused by a virus known as Measles virus which is an RNA virus of the family Paramyxoviridae and Genus Morbilivirus. Measles virus is an enveloped virus with a non-segmented, negative sense, single stranded RNA as its genome. Measles virus is monotypic, but genetic variation in the haemagglutinin (H) and nucleoprotein (N) genes can be analyzed by molecular epidemiologic techniques and used to study virus transmission patterns. The World Health Organization currently recognizes 8 clades (A-H) within which are 24 genotypes of measles virus and one provisional genotype, d11. Genotype B3 is clearly the endemic genotype in most parts of African continent where it is widely distributed (Demanou *et al.*, 2013).

The virus is known to cause disease only in humans and is highly infectious. Measles causes immunosuppresion that persist for weeks to months after the acute infection. This may predispose individual to severe bacterial infections (Coetzee, 2013). Complications of Measles have been reported in every organ system. Some of the complications of the disease are Pneumonia, croup, and encephalitis. Encephalitis is the most common cause of long-term sequelae and death. Measles remain the most common cause of blindness in developing countries. Complications are higher in those less than five and greater than 20 years old, although croup and otitis media are common in those less than two and encephalitis in older children and adults (Perry and Haisey, 2004).

Predisposing factors to the measles infection have been reported to be among others, malnutrition and tuberculosis (WHO, 2001). Others that are at risk of being infected include unvaccinated children, infant who lost passive immunity prior to the age of routine immunization, and children with immunodeficiency (Coetzee, 2013).

Measles is considered an eradicable disease due to the single serotype, effective vaccine, lack of naturally occurring non-human reservoirs and high clinical expression of the disease. The high communicability of measles infection, its resemblance in the prodromal stage to other febrile rash diseases, and the occasional occurrence of asymptomatic and non-classical cases are seen as challenges which can be surmounted (WHO, 2000).

Immunity against Measles can be achieved through vaccination and can also be produced in individuals who had the disease and successfully recovered or as passive immunity in neonate as a result of Maternal Measles Antibodies (MMAs) which may wane sometimes even before the age of receiving the first dose of the vaccine. This renders them vulnerable to infection by the measles virus (CDC, 2015). Although, measles immunization is widely regarded as one of the safest and most cost effective public health interventions, serological studies indicated that vaccine-induced immunity might be less protective and less durable than immunity conferred by natural measles infection (Mossong and Muller, 2013). This brought about the idea to determine the prevalence of measles IgG antibody among children, base on their history of the infection.

MATERIALS AND METHODS
Study Area
The research was carried out in Adamawa State, located in North Eastern part of Nigeria, with its capital at Yola. The state has a land mass of 39,742.12 sq km, and population of 3,106,585 (2005 estimate.). It is situated between 80^0 N and 11^0N and longitude 11.5^0 and 13.5^0 E. It shares boundaries with Gombe State to the North, and Borno State to the North East. While to the West it is bordered with Taraba State as well as the Republic of Cameroon to the East (web).
Sampling Techniques
Multistage sampling technique was used to draw the samples for this study.
Stage 1; Cluster sampling was used to cluster the state into three based on senatorial zones of the state.
Stage 2; Random sampling was used to select two Local Government Areas (L.G A) from each of the senatorial zone making six Local Government Areas.
Stage 3; Hospitals, nursery, primary and junior secondary schools were randomly selected from each of the selected Local government Areas.
Stage 4; Stratified sampling was used to select the children between 0-14 years based on the age group 0-4; 5-9; 10-14 for convenience.
Sample Size Determination
 In order to obtain an appropriate sample size that will represent the total number of children aged 0-14 years in the state, and their respective number in the various Local Government selected for the study, the following formular was used.

$$n = \frac{Z^2 (P) (1-P)}{d^2} \quad \text{(Naing } et\ al.,\ 2006)$$

Going by the formular, at confidence level of 95%, a sample size of 349.5 is required for the study but 400 samples were collected as a precaution in case of any sample damage during transportation and storage. However 368 were used. Sample size from each Local Government selected was determined by stratification according to age groups (0-4, 5-9, and 10-14).
Ethical Consideration
Approval was obtained from Adamawa State Hospital Service Management Board (Ref. No. HSMB/S291 Vol.1/11), and Adamawa State Universal Basic Education Board (Ref. No. UBEB/SS/280/VOL.1). Also, informed consent approval was obtained from parents of the participating population before collecting samples.
Demographical Data of the Participants
Questionnaire methods were employed to obtain demographical data of the participants. The questionnaires were filled with the demographical data of the participants such as gender, age, history of measles infection, parents' occupation, and type of settlement and history of vaccination. This was done prior to collection of samples.
Sample Collection
With the help of professional health personnel, 2-3 millilitres (ml) blood samples were collected from the participants depending on their age, by using venipuncture using sterile disposable syringe and needles. The samples were then transferred in to sterile centrifuge tubes that were appropriately labelled. On arrival to the laboratory, the blood samples were allowed to clot and then centrifuged at 2000rpm for 5 minutes, the sera were harvested into clean sterile screw capped bottles with proper label (WHO, 2000).
Sample Analysis
Sample sera were assayed using measles IgG commercial ELISA kit (Demeditect, 2015) manufactured by Demeditec Diagnostics GmbH. Lise-Meitner-Straße 2. D-24145 Kiel (Germany) in accordance with the manufacturer's instructions and the standardised laboratory procedure to determine the measles IgG antibody qualitatively and quantitatively.

RESULTS
Occurrence of Measles IgG Antibody Titres in the Study
   Quantitative measles IgG antibody titres obtained in this study by Indirect ELISA plate method were <1 to > 250 U/mL. Antibody titres of ≤ 9 U/mL were considered negative (non-protective) while ≥ 10 U/mL were considered positive (protective).

According to the kit manufacturer's instruction, antibody titre of 10 U/mL is the cut-off titre, >10 - 40 U/mL were regarded as weak positive, while >40 - ≥ 250 U/mL were regarded as strong positive.

From all the six local governments in the study, 141 (38.4%) out of 368 study participants had non-protective antibody titre, 118 (32.1%) had the cut- titre, 95 (25.8%) had weak positive titres while only 14 (3.8%) had strong positive titres among which 5 were from Girei L.G.A and none from Numan as shown in Table 1.

Table 1: Measles ELISA IgG Antibody Titres of Children in Six L.G.A of Adamawa State

L.G.A	Antibody titre (U/mL)				
	<10	10	>10 - 40	>40 - ≥250	Total
	Number of children / (%)				
Yola South	28(31.5)	30(33.7)	28(31.5)	3(3.3)	89(100)
Girei	20(33.4)	11(18.3)	24(40.0)	5(8.3)	60(100)
Mubi north	27(39.7)	28(41.2)	10(14.7)	3(4.4)	68(100)
Maiha	28(43.8)	21(32.8)	14(21.9)	1(1.5)	64(100)
Ganye	19(40.4)	17(36.2)	9(19.1)	2(4.3)	47(100)
Numan	19(47.5)	11(27.5)	10(25.0)	0(0.0)	40(100)
Total	141(38.4)	118(32.1)	95(25.8)	14(3.8)	368(100)

Prevalence of Measles Specific IgG Antibody Based on Age and Gender

Table 2 showed Antibody status against measles among children in Adamawa based on age and gender. Overall result showed that out of 368 children from all age group and gender, 227 (61.6%) had protective antibody against measles while 141(38.4%) had non-protective antibody. Out of 70 male and 73 females aged 0-4, 47(67.1%) and 50 (68.4%) respectively had protective antibody while 23(32.9%) male and 23(31.6%) female had non-protective or negative antibody. Among children aged 5-9 years, 42(60.0%) male out of 70 and 24(51.0%) female out of 47 had protective antibody while the remaining 28(40%) male and 23(49%) female had non-protective antibody. At the age group 10-14, 34(57%) male out of 59 and 30(61.2%) female out of 49 also had protective antibody but the remaining 25(42.4%) male and 19(38.8%) female had non-protective antibody against measles. Chi-square test showed that there is no significant association between age and antibody status (p-value 0.140), and also between gender and antibody status (p-value 0.958) as there is no gender or age group that is more protective than the other.

Table 2: Antibody (Immunity) Status against Measles among Children Based on Age and Gender

Age group (years)	Gender	Antibody Status		
		Protected	Non-protected	Total
0-4	M	47(67.1%)	23(32.9%)	70
	F	50(68.4%)	23(31.6%)	73
5-9	M	42(60.0%)	28(40.0%)	70
	F	24(51.0%)	23(49.0%)	47
10-14	M	34(57.6%)	25(42.4%)	59
	F	30(61.2%)	19(38.8%)	49
Total		227(61.6%)	141(38.4%)	368

Pearson Chi-square =3.9325, p-value =0.140 and 0.0028, p-value = 0.958 for age and gender respectively.

Prevalence of Measles Specific IgG Antibody Based on History of Measles Infection

Table 3 showed antibody status of the children based on their history of measles infection and 83(22.6%) of the 368 children enrolled in this study had history of measles infection while 285(77.4%) had no history of measles. Among those with history of measles infection, 80(96.4%) had protective antibody while 3(3.6%) had non-protective antibody. Of those with no history of measles, 147(51.6%) had protective antibody while 138(48.4%) of them had non-protective antibody.

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Among the age group 0-4 years, 25(92.5%) of those with history of measles had protective antibody while 2(7.5%) of them had non-protective antibody and 72(63.7%) of those with no history of measles had protective antibody while 41(36.6%) of them had non-protective antibody.

At the age group 5-9years, 24(96%) of those that had measles were having protective antibody titre while only 1(4%) had non-

protective antibody titre. And among those with no history of the disease, 42(46.2%) had protective antibody and 49(53.8%) had non-protective antibody.

All the 31(100%) of those with history of measles aged 10-14 years had protective antibody and 33(40.7%) of those without history of measles had protective antibody while 48(59.3%) of them had non-protective antibody as shown in table 3.

Table 3: Measles Antibody (Immunity) Status Based on History of Measles Infection

	Had measles			Had no measles	
	Protected	Non-protected		Protected	Non-protected
Age group	(%)	(%)		(%)	(%)
0-4	25(92.5)	2(7.5)		72(63.7)	41(36.3)
5-9	24(96.0)	1(4.0)		42(46.2)	49(53.8)
10-14	31(100)	0(0.0)		33(40.7)	48(59.3)
Total	80(96.4)	3(3.6)		147(51.6)	138(48.4)

Pearson Chi-square = 54.6021, P-value = 0.000

DISCUSSION

The result of the study indicated that majority of the children 227(61.6%) had protective (positive) antibody against measles while 141(38.4%) had non-protective (negative) antibody. Antibody titre ≥ 10 U/ml was considered protective. The large number of children with protective antibody titre may be due to the fact that there was a wide range of vaccination coverage against measles in the State ranging from 61% in 2005 to 99% in 2008 as reported by Weldegebriel *et al.,* (2011). It may also be attributed to the significant number of children 83(23%) who had the disease (from their history), and must have acquired the antibody as a result of active immunity. Among those with protective antibody titre, 118 (32.1%) were having the cut-off titre of 10U/ml but plus or minus 20% of the cut-off titre is regarded as grey zone. This therefore, shows that these children are on their way to either losing or obtaining protective antibody titre as indicated in the ELISA kit's manual. Also, 95 (25.8%) of those with protective titre were having weak positive titre and only 14 (3.8%) had strong positive titre. This may probably be due to waning of vaccine induced antibody as well as lack of re-exposure to the measles virus. This is because studies have shown that vaccine induced immunity decline over time and sub-clinical boosting of antibody levels may result from frequent exposure to measles virus in regions where the virus is circulating as suggested by Whittle *et al*. (1999). The study also showed that 141 (38.1%) of children enrolled in the study had non-protective antibody titre. These may be those with no history of being infected with measles virus, the non-vaccinated, those

that were vaccinated but failed to respond to the vaccine as a result of several factors and those that lost their vaccine immunity as a result of antibody waning. In comparism with the above findings, a serological evaluation of immunity against measles in children attending Murtala Mohammed Specialists Hospital, Kano-Nigeria conducted by Hamid *et al.,* (2012) revealed that majority of the children had protective HI antibody titre (65.6%), while few (34.4%) had either undetectable antibody or low levels of HI antibody titre, which will not confer protection. The study also revealed that there was significant association between measles infection and protection against measles among the children at P<0.05. Also a community-based survey to determine the prevalence of measles HI antibodies among children in Santa Cruz Bolivia was conducted by Bartoloni *et al*. (2004) reported that measles vaccine coverage in the children was 77% and 1439 (87%) had detectable HI antibody, but a high proportion had antibody levels below 200miu (30-40%).They associated measles seronegativity with not being vaccinated against measles, negative history of measles disease and young age. Of the 212 children without detectable measles antibody, 123 (58%) had a positive history of vaccination or measles disease, they noted that historical information was not sufficiently reliable to identify susceptible. These two findings are in conformity with the finding of the present study. However, different antibody detection methods were used and there is disparity pertaining protective titres which depends on methods and detection kits used

The present study also showed that there was no significant relationship between prevalence of measles specific IgG antibody and gender as well as the age of the children (p>0.05). But according to WHO (2008), several studies reported intriguing sex differences in the immunogenicity and reactogenicity of measles vaccine, with higher post-vaccination antibody levels and rates of fever and rash in girls. Interest in sex differences in response to measles vaccine was stimulated by reports of increased mortality in girls following receipt of the high-titre measles vaccine. However, sex differences in seroconversion rates were not reported in the majority of studies on the immunogenicity of standard-titre measles vaccine. The immunological basis for any sex differences in the responses to measles vaccines is not known (WHO, 2008). Among these studies was the study on Gender differences in the reactogenicity of measles-mumps rubella vaccine by Shohat *et al.,* (2000), whose findings demonstrated higher rates of adverse effects in females following vaccination with MMR vaccine, the relative risk of fever and rash following vaccination was 2.35 in females and 1.36 in males, but he geometric mean antibody titres against measles were similar in both sexes and there was no significant association between antibody titre and post-vaccination morbidity in either sex.

Similar to those studies was the study on the influence of sex and gender on immunity, infection and vaccination conducted by Anna *et al.,* (2016) which showed that Sex/gender significantly contribute to shape the immune responses, contributing to differences in the pathogenesis of infectious diseases in males and females, the response to viral vaccines and the prevalence of autoimmune diseases. Females typically develop higher innate, humoral and cellular immune responses to viral infections and in response to vaccine. At the same time, women are more prone to autoimmune diseases and experience more adverse reactions to vaccination. Hormonal, genetic and environmental factors between males and females may affect the immune responses and the sex-related outcome of vaccination.

Although, the duration of protection following measles virus infection is generally thought to be lifelong, astoundingly, 3(3.6%) of those who had history of measles were not-protected. This may be due to low antibody titre which was undetected and the children were probably not re-exposed to the measles virus after the first exposure. Consequently, the antibody level may become undetectable until when re-exposed again. This is in agreement with the work of Hamid *et al.,* (2012) were 16.52% of those with history of measles infection were not protected. He also stated that when measles antibody falls to low levels, re-exposure to measles virus (wild or vaccine virus) stimulate memory cells, which remain dormant after the initial infection and primed to produce a measles specific response. Or it may be that their history of measles disease has been mistaken with other febrile rash illnesses such as rubella, dengue fever, coxsackie, bacterial and rickettsial diseases. This is in line with the WHO, (2000) report that the non-specific nature of the prodromal signs and the existence of mild cases make clinical signs unreliable as the sole diagnostic criteria of measles disease. As disease prevalence falls, many medical practitioners will be inexperienced in recognizing measles and the need will increase for laboratory methods of distinguishing measles from other clinically similar diseases.

CONCLUSION

The study revealed that majority of the children had protective antibody titre, while few had either no or undetectable antibody (low levels antibody titre) which will not confer protection against measles. The study also revealed that at 95% confidence level, there was a significant relationship between prevalence of measles IgG antibody and history of measles infection (p<0.05) but there was no significant relationship between the prevalence of measles IgG antibody with age and gender (p>0.05). Therefore, this study revealed that the immunity (prevalence of measles IgG antibody) in the state is less than the herd immunity required to prevent sustained transmission of the disease and higher level of immunity need to be achieved in order to prevent the spread of the virus.

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