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Seroprevalence of Measles Virus among Children 0–12 Years of Age in Some States in North Western Nigeria

K. Abdulfatai[1*], O.S. Olonitola[2], M. Aminu[2] and E.D. Jatau[2]

[1]Department of Microbiology, Kaduna State University, Kaduna, Nigeria
[2]Department of Microbiology, Ahmadu Bello University, Zaria, Nigeria
**Corresponding author*

A B S T R A C T

Serological Survey of measles virus among children 0 – 12 years of age was carried out in some States in North Western Nigeria. A total of 450 blood samples were collected and analyzed for measles virus IgM and IgG using commercial Elisa kit Obtained from Diagnostic Automation/ Cortez Diagnostics, California, the results was interpreted according to the manufacturer’s instruction. The data was analyzed using statistical package for social sciences (SPSS) Version 21. Of the total number of 450 samples analyzed for Measles Virus Infection IgM and IgG antibodies, 158(35.10%) were seropositive for IgM and 385 (85.60%) were seropostive for IgG. In relation to the age group for measles virus IgM, age group 1 – 5 years had the highest seroprevalence of 96(47.80%), followed by age group < 1 years with the seroprevalence of 25(31.25%). Age group 11 – 15 years had the least seroprevalance of 8(11.90%). There was statistically significant association (P- value 0.000 < 0.05). For measles virus IgG, in relation to the age group, age group 1 – 5 years had the highest seroprevalance of 195(97.07%), followed by age group 6 – 10 years with the prevalence of 95(93.14%). Age group <1years had the least seroprevalance of 40(50.00%). In relation to sex for IgM, male children had the highest seroprevalence of 83(35.80%) and female children had the seroprevalence of 75(34.40%). While for IgG antibody in relation to sex male children had the seroprevalance of 198(85.31) and female children had the seroprevalance of 187 (85.77). This study recognized age, Nutritional Status of children, Parent Socio-economic status, Parent Occupation, Parent Education, vaccination status of children and Vitamin A Supplement intake as important demographic and risk factors of measles virus infection in children.

Keywords

Measles virus infection, Aerosolized secretions, Maculopapular rash, Systemic infection, Respiratory epithelium, Nasopharynx, viremia, Otitis media, Pneumonia.

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Introduction

Measles virus belonging to the genus *Morbillivirus* in the family *Paramyxoviridae* is an enveloped virus with a non-segmented, negative-strand RNA genome (Griffin, 2001). It is 100 – 200 nm in diameter and two membrane envelope proteins are important in pathogenesis which are the F (fusion) protein, which is responsible for fusion of virus and host cell membranes, viral penetration, and hemolysis, and the H (hemagglutinin) protein, which is responsible for adsorption of virus to cells (Bellini *et al.*, 2005).

The World Health Organization (WHO) currently recognizes 8 clades designated A, B, C, D, E, F, G, and H. Within these clades, there are 23 recognized genotypes, designated A, B1, B2, B3, C1, C2, D1, D2, D3, D4, D5,

D6, D7, D8, D9, D10, E, F, G1, G2, G3, H1, and H2, and one provisional genotype, d11 (WHO, 2015).

In order to infect a cell, a virus must first bind to a cellular receptor on the surface and enter the cell. The presence of such a receptor determines whether the cell is susceptible to the virus. Measles is a highly infectious disease characterized by fever, respiratory symptoms, redness of the eyes and a maculopapular rash. Complications are common and may be quite serious. The rash usually starts on the head and then spreads to the rest of the body. Fever can persist, reaching extremely high temperatures, rash can last for up to a week, and coughing can last about 10 days (Jawestz *et al.*, 2011).

The causative agent of measles virus is generally transmitted by aerosolized secretions deposited on upper respiratory tract mucosal surfaces. Exposure leads to local respiratory tract replication; infection of regional lymphoid tissues then occurs followed by viremia and systemic dissemination as revealed by the characteristic skin rash. Most children recover uneventfully from the illness, but serious complications can occur, including pneumonia and involvement of the central nervous system (Parks *et al.*, 2009).

Airflow studies demonstrated that droplet nuclei generated in the examining room used by the source patient were dispersed throughout the entire office suite. Airborne spread of measles from a vigorously coughing child was the most likely mode of transmission (Bloch *et al.*, 2005).

Measles is a systemic infection and the primary site of infection is the respiratory epithelium of the nasopharynx. Two to three days after invasion and replication in the respiratory epithelium and regional lymphnodes, a primary viremia occurs with subsequent infection of the reticuloendothelial system. Following further viral replication in regional and distal reticuloendothelial sites, a second viremia occurs 5–7 days after initial infection. During this viremia, there may be infection of the respiratory tract and other organs. Measles virus is shed from the nasopharynx beginning with the prodrome until 3–4 days after rash onset (Gerber *et al.*, 2009).

Prevention of measles infection rests on successful immunization with currently available live, attenuated vaccine. The immunity produced by the vaccine lasts many years and is probably life-long. The recommended age of administration in infant immunization programmes is 9 to 15 months. Vaccine efficacy is 85% at 9 months of age and increases to 90–95% at 12–15 months of age. Measles virus is highly transmissible. High routine immunization coverage can reduce measles incidence but will not prevent accumulation of susceptible individuals, which can lead to outbreaks if virus is introduced into a population where the number of susceptible individual are above the critical threshold for that population (WHO, 2010).

The use of vitamin A in treatment has been investigated. A systematic review of trials into its use found no significant reduction in overall mortality, but it did reduce mortality in children aged less than two years (Souza *et al.*, 2002)

Five out of six WHO regions have set goals to eliminate measles, and at the 63rd World Health Assembly in May 2010, delegates agreed to a global target of a 95% reduction in measles mortality by 2015 from the level seen in 2000, as well as to move towards eventual eradication. However, no specific global target date for eradication has yet been agreed (WHO, 2010).

Materials and Methods

Study area

The study was conducted in some North Western region of Nigeria. Sokoto, Jigawa and Kaduna State

Study population

Children 0-12 years of age with suspected measles symptoms like, fever of 38^0 C or greater, cough, redness of the eyes and maculopapular rash, attending selected hospitals in the study area were included.

Sample size

A convenience sampling technique was employed; therefore, 450 blood samples of children attending some selected hospital in the North western Nigeria were collected**.**

Structural questionnaire

The parents or care givers of the children under study were given a letter of introduction seeking their consent and a detailed questionnaire to record: Demographic data, Age, Sex, previous history of measles vaccination and recurrent cases.

Sample collection and analysis

Blood samples were collected aseptically from each clinical case children by an experienced technician and dispensed into sterile labeled plain specimen bottles. Measles specific IgM and IgG antibodies in serum were detected by enzyme immunoassay (Diagnostics Automation, U.S.A) in accordance with the manufacturer's instruction as follows: 100µl each of the dilutions were dispensed into appropriate wells, and incubated at room temperature for 30minutes. After incubation, the wells were washed three times with washing buffer, excess washing solution were removed by gentle tapping on a tissue cloth, this was followed by the addition of 100µl enzyme conjugate and incubation at room temperature for 30 minutes, the same initial washing steps was followed to remove excess conjugate, the substrate were then dispensed into the wells and incubated for 20mins at room temperature, finally the reaction was stopped by addition of 100ul stop solution and the resulting reaction was read at 450nm using ELISA reading machine.

Data analysis

Data were analyzed using SPSS (software version 20) to determine association between demographic factors and risk factors respectively.

Results and Discussion

Out of the total 450 blood samples screened for the presence of measles virus IgG and IgM antibody in children 0 – 12 years of age 385 (85.6%:385/450) were positive for measles virus IgG and 158 (35.170:158/450) were positive for measles virus IgM antibody (Table 1), Children in Sokoto state had the highest seroprevalence of IgG and IgM (50.7%:76/150) compared to children in Kaduna with a lower seroprevalence (21.3%:32/150) (Tables 1 and 2).

Measles virus was detected in all age groups with the highest IgG prevalence of 97.0% (195/201) and IgM prevalence of 47.8% (96/201) occurring in children of age group 1 – 5 years old. Children in age group <1 years old had the least prevalence of 52.0% (40/80) for measles IgG antibody and children in age group 11 – 15 years old had the least prevalence for measles virus IgM antibody, 11.9% (08/67). This is presented in figure 1.

The seroprevalence of measles virus IgG and IgM with respect to sex of the children was observed to be higher in male children with the prevalence of 85.7% (199/232) for measles IgG and 35.8% (83/232) for measles IgM respectively and lowest in female children with the prevalence (85.3%:186/218), (34.4%:75/218) (Figure 2).

Seroprevalence of measles virus infection in children with respect to parent's educational status, parent with no formal education had the highest seroprevalence (62.8%: 71/113) compared to children whose parents had tertiary education (6.6%:04/61).

Highest prevalence (45.2%:121/280) was observed in children whose parents were civil servant and the least prevalence (21.7%:37/170) in children whose parents were self-employed. Parents with low socio economic status had the highest seroprevalence (43%:101/235) compared to parents high socioeconomic status with the least prevalence (20.7%:24/116). Highest prevalence was recorded in children with poor nutritional status (40.8%:98/240) and children with normal nutritional status had the least seroprevalence (22%:26/118) (Table 3).

Highest prevalence was observed in children with not sure of taking vitamin A supplement (48.4%:91/188) and lowest prevalence was observed in children who were given vitamin A supplement (13.9%:14/101). This is presented in table 4.

Children who have fever had a higher prevalence of 27.4% (78/285) compared to children who did not have fever (14.6%:24/165). Children who were coughing had the highest prevalence (29.7%:65/219) compared to children that were not coughing with the least prevalence (10.8%:25/231). Children who had diarrhea had a higher prevalence (28.1%:81/295) compared to children who did not have diarrhea with a lower prevalence of 20% (31/155). Children that were vomiting had the highest prevalence of 25.4% (75/295) compared to children that were not vomiting (18%:28/155). Children that had rash on their body had the highest prevalence of 80.2% (81/101) compared to children who did not have rash (17.8%:62/349). Children with conjunctiva had the highest prevalence of 21.4% (21/98) compared to children without conjunctiva (14.8%:52/352) (Table 5).

Children who were not vaccinated had the highest prevalence of 61.7% (84/141) compared to children who were vaccinated with the least prevalence (22.9%:71/309). This is presented in table 6.

The high positive rate of measles IgG antibodies compared to IgM may be due to previous infection or vaccination of the children. 35.1% of sero positive cases of measles IgM antibodies in this study were from children who may have been unimmunized with the measles vaccine or had an incomplete course of the routine vaccination. The result agrees with 32.2% recorded in Kaduna state, Nigeria (Chechet *et al.*, 2014), and 34% reported in Abia state, Nigeria (Nguku *et al.*, 2012) However the prevalence contradicts 19% reported in Oshogbo, Osun state (Adetunji *et al.*, 2010), 21.4% reported in Senegal and 62.8% reported in India (Wairagkar *et al.*, 2011).

The highest and lowest seroprevalence of measles IgG and IgM antibodies seen in Sokoto and Kaduna States respectively, which may be attributed to geographical and environmental factors, most especially the humidity of the area.

This agrees with the finding of James *et al.*, (2011) on the geographical changing epidemiology of measles in Africa.

The high presence of IgG antibody to measles virus in age group 1 – 5 years may be due to previous exposure to the virus through vaccination or infection. It could also be as a result of the closeness of the age group to the vaccination age. The high prevalence of IgM antibody to measles virus in the same age group 1 – 5 years may be due the inability of the IgG antibody to prevent against second infections. The high prevalence of IgM observed is in agreement with the prevalence of 55% recorded in a study in Lagos (Adetunji *et al.,* 2007), 69.61% reported in Bolvia (Automated *et al.,* 2013). The reason for the observed decline in the seroprevalence of IgM with age may be attributed to the proper measles vaccine immunization coverage in Nigeria. Accelerated measles control programme including improved provision of a second dose of measles vaccine at supplementary vaccination activities in certain countries of the world and case based surveillance with laboratory confirmation may have reduced measles associated morbidity and mortality (Manirakiza *et al.,* 2012). This study also revealed that children < 1year in the North Western Nigeria are more susceptible to measles virus infection. This may be due to failure to received vaccine against measles infection or the early waning of transplacentally acquired immunity which made the pre-vaccination age infants more vulnerable. Positive cases of measles decreases as the age of the children increased This may be attributed to the physiological status of the individual child and variation in prevailing environmental factors (Akramuzzaman *et al.,* 2010), in addition, immunity acquired by older children over the years as a result of sub clinical infections might provide the required protection against measles (Patel *et al.,* 2009).

It was also observed from this study that children 1 – 5 years of age were more likely to be infected with measles virus. This is in agreement with previous study which shows that 58% of infants loose there protective antibodies by four months and 97% between seven and nine months (Oyedele *et al.,* 2005, Nishoe *et al.,* 2013, Ismail *et al.,* 2014).

Table.1 Seroprevalence of measles IgM and IgG antibody in the selected hospitals within the North Western Nigeria

Hospitals	**N**	**IgM Positive (%)**	χ^2	**P-Value**	**IgG Positive (%)**	χ^2	**P- Value**
YDMH	75	25 (33.3)	80.371	0.000*	68 (90.7)	32.458	0.000*
RGH	75	07(09.3)			55 (73.3)		
DSH	75	25 (33.3)			56 (74.7)		
GHD	75	25 (33.3)			74 (98.7)		
WCWC	75	19 (25.3)			62 (82.7)		
SSH	75	57(76.0)			70 (93.3)		
Total	**450**	**158(35.1) (35.10)**			**385(85.6) (85.60)**		

IgM: χ^2 =80.371, df =5, p=0.000* IgG: χ^2 =32.458, df =5, p=0.000*

KEY: n = Number of subjects Tested, (%ve) = Percentage positive, χ^2=Chi-Square, df= Degree of freedom, p=P-value, YDMH, Yusuf Dantsoho Memorial Hospital, RGH = Rigasa General Hospital, DSH = Danmazara Specialist Hospital, GHD = General Hospital Dutse, WCWC = Women and Children Welfare Center and SSH = Sokoto Specialist Hospital.

Table.2 Seroprevalence of measles IgM and IgG antibody within the states in the North Western Nigerian

State	N	IgM n (%)	IgG n (%)	IgM and IgG n (%)
Sokoto	150	76(50.7)	132(88.0)	76(50.7)
Jigawa	150	50(33.3)	130(86.6)	50(33.3)
Kaduna	150	32(21.3)	123(82.0)	32(21.3)
Total	**450**	**158(35.1)**	**385(85.6)**	**158(35.1)**
χ^2		**28.637**	**2.410**	**28.637**
P – Value		**0.000**	**0.0002**	**0.000**

Key: N= Number Examined, n= Number Positive, %=Percentage Prevalence, IgM= Immunoglobulin M, IgG=Immunoglobulin G, χ^2=Chi-Square value

Table.3 Seroprevalence of measles IgM antibody in relation to some socio – demographic factors

Factor	Number Tested	Seropositive (%)	χ^2	P – value
Parent's educational Status				
Primary	115	61 (53.0)	108.677	0.000
Secondary	161	22 (13.7)		
Tertiary	61	04 (06.6)		
Non – Formal	113	71 (62.8)		
Parent's Occupation				
Self Employed	170	37(21.8)	21.361	0.000
Civil Servants	280	121(43.2)		
Parent Socio –Economic Status				
High Status	116	24 (20.7)	17.111	0.000
Middle Status	99	33 (33.3)		
Low Status	235	101 (43.0)		
Nutritional Status of child				
Normal	118	26 (22.0)	12.444	0.002
Average	92	34 (36.9)		
Poor	240	98 (40.8)		
Total	**450**	**158(35.1)**		

Key: % Percentage, P level of Significance

Table.4 Seroprevalence of measles IgM antibody in relation to vitamin A supplement intake

Vit.A Supplement	Number Tested	Seropositive (%)	χ^2	P - Value
Yes	101	14 (13.9)	34.939	0.001
No	161	53 (32.9)		
Not Sure	188	91 (48.4)		
Total	**450**	**158 (35.1)**		

Key: Vit – Vitamin, % - Percentage

Table.5 Seroprevalence of measles IgM antibody in relation to symptoms of disease

Symptoms	Response	Number of Subject Tested	Seropositive (%)	χ^2	P – Value
Fever	Yes	285	78 (27.4)	9.803	0.002
	No	165	24 (14.6)		
Cough	Yes	219	65 (29.7)	24.987	0.000
	No	231	25 (10.8)		
Diarrhea	Yes	295	83 (28.1)	3.555	0.059
	No	155	31 (20.0)		
Vomiting	Yes	295	75 (25.4)	3.118	0.077
	No	155	28 (18.0)		
Rash	Yes	101	81 (80.2)	140.836	0.000
	No	349	62 (17.8)		
Conjunctiva	Yes	98	21 (21.4)	2.499	0.004
	No	352	52 (14.8)		

Key: % = Percentage, P = Level of Significances

Table.6 Seroprevalence of measles IgM antibody in relation to vaccinated and non vaccinated children

Vaccination Status	Number Tested	Seropositive (%)	χ^2	P - value
Vaccinated	309	71 (22.9)	63.728	0.000
Non – Vaccinated	141	87 (61.7)		
Total	**450**	**158 (35.1)**		

Key: % = Percentage, P = Level of Significances

Figure.1

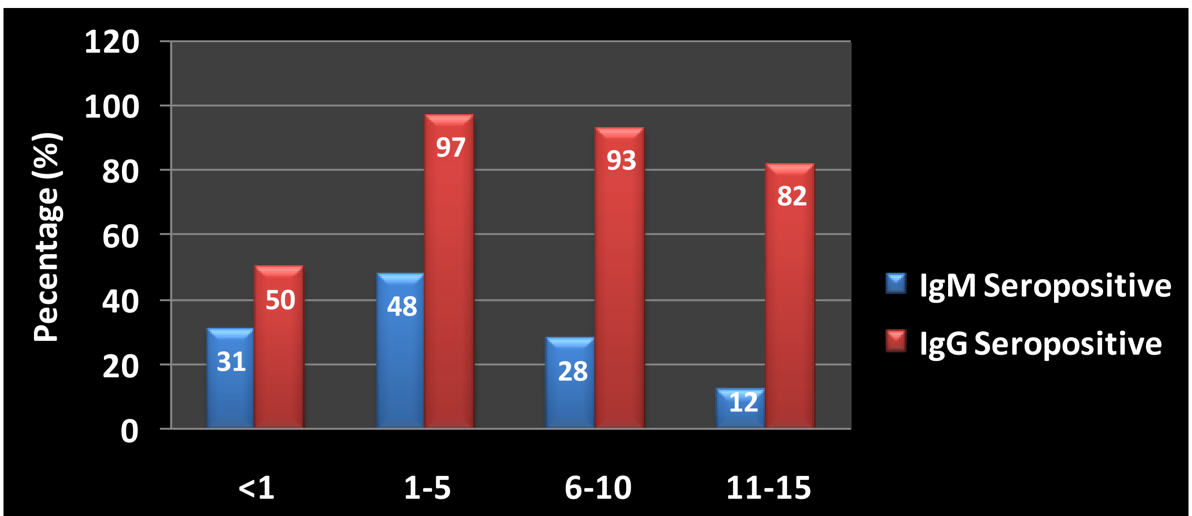

Fig. 1: Seroprevalence of Measles IgM and IgG Antibodies in Relation to Age Groups within the Selected Hospitals

Figure.2

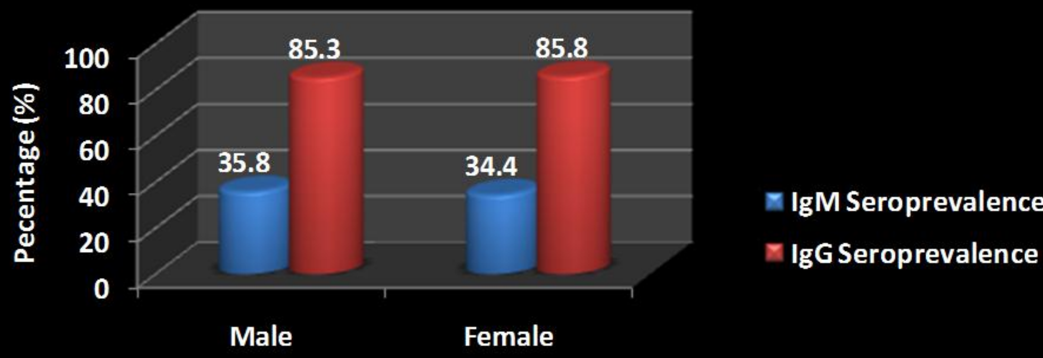

Fig2: Seroprevalence of Measles IgM and IgG Antibodies in Relation to Gender in the Selected Hospitals

The second peak age of presentation of measles virus occurred in the second year of life (Onyiruka *et al.*, 2011, Ahmed *et al.*, 2010), the reasons for this disparity is unclear but the finding of about 31.25% in all affected children age less than 1 year (< 1) in this research has been attributed to a rapid declined in maternally acquired antibodies which some author reported was due to the presence of other infections (Fetuga and Njokanma *et al.*, 2007) and malnutrition (Odoemele *et al.*, 2008).

The prevalence of IgM antibodies against measles virus observed in age groups 6-10 and 11-15 years may be due to a shift of the infection to older age groups if past immunization efforts had been weak implying that older unimmunized children may still be susceptible to new infection.

This agrees with the finding of Wichmann *et al.*, (2009) who reported a shift in the distribution of cases to older children.

The high seroprevalence of measles virus IgG antibodies in relation to Gender may be attributed to previous vaccination or incomplete course of routine vaccination in both sexes.
This result is in agreement with previous study in Nigeria (Bassey *et al.*, 2010; Aumatel *et al.*, 2013) which reported that measles antibody is marginally higher in male than in their female.
Seroprevalence of measles virus IgM in relation to socio demographic factors shows a significant association between parent levels of education and measles virus. The high seroprevalence in children of parents with non – formal and primary education may be due to the parent's ignorance on the need for measles vaccination. Studies had shown that educated women are more concerned with the immunization of their children and proper immunization schedules than uneducated women (Muhammed and Danish, 2014). This is also similar with the findings of Aumatel *et al.*, (2013) where seroprevalence of measles virus was higher in children of mothers with less than secondary educational level but lower in children of mothers with highly educational level. Children of parents who are self-employed had the lower seroprevalence while children of parents who are civil servant had the highest seroprevalence. These differences could be as result of the time spent on child care since civil servant spend more time at work than on other things and may possibility miss the routine immunization of their children. This finding agrees with a study carried out in United State where children of working class parents were more susceptible to infection (Holmes *et al.*, 1996).

Parents with low economic status had the highest seroprevalence followed by parents with Middle economic status and parenst with high economic status had the least seroprevalence. This may be due to more crowded living conditions and poorer hygiene among the low socioeconomic status. This agrees with the finding of Saleh, (2016) trends of measles in Nigeria

The Nutritional status of children was also assessed and children with poor nutritional status has the highest seroprevalence followed by children with average nutritional status and the least seroprevalence as observed in children with Normal Nutritional status. This agrees with the finding of Augoye, (2012) which is corroborated by the claim of about a quarter (27%) parents in Nigeria that their children go without food for a day, according to a survey conducted by charity save the children group.

Seroprevalence of measles IgM antibody in relation to Vitamin A Supplement intake shows significant associations between vitamin A supplement intake and measles virus infection. Children that were giving Vitamin A supplement had the least seropositive and children with no intake of vitamin A supplement had a higher seroprevalence. Concurrent vitamin A deficiency increases rates of complications. This agrees with the finding of Okada *et al.,* (2012) who reported that vitamin A supplementation, and antibiotic therapies for secondary infections have reduced measles-associated deaths in the developing world.

Seroprevalence of measles IgM in relation to symptoms of Disease, this study observed that all symptoms, fever, cough, conjunctiva and rash had a significant association with measles virus infection. Diarrhea and vomiting was however not statistically signification. This agrees with WHO (2013) on clinical case definition of measles virus symptoms, any child presently with a history of fever (38 to 40^{o}C) lasting three days or more and generalized Rash with one of the following, Cough or Conjunctivitis. It also agrees with the finding of Jawestz *et al.,* (2011) who reported that Measles is a highly infectious disease characterized by fever, respiratory symptoms, redness of the eyes and a maculopapular rash. Complications are common and may be quite serious. The rash usually starts on the head and then spreads to the rest of the body. Fever can persist, reaching extremely high temperatures, rash can last for up to a week, and coughing can last about 10 days.

Seroprevalence of measles virus in relation to vaccinated and non-vaccinated children shows a statistically significant association between measles virus infection and vaccination. Vaccinated children had the least seroprevalence while t unvaccinated children had the highest seroprevalence. This agrees with the finding of Aaby *et al.,* (2012) on the policy of measles vaccination at 9 months was based on various studies on sero-conversion after measles vaccination at different ages. Expanded Programme on Immunization recently recommended by WHO is that all children should receive 2 doses of measles containing vaccine(MCV); the first dose during the routine immunization programme and the second dose either through routine services or through Supplemental immunization activities(SIAs) (Danet and Fermon, 2013)

In conclusion, the burden of measles in Nigeria remains high despite global efforts targeted at elimination, with infants and the unvaccinated being the most susceptible. The findings in the study confirmed the presence of Measles virus in children (0-12years of age) in the North Western Nigeria, with seroprevalence comparable to the rates obtained in other parts of the country. The prevalence of 35.1% was obtained for IgM antibody and 85.6% was obtained for IgG. This is an indication that measles is endemic in the North Western Nigeria and still poses a public health problem, despite the availability of a safe and effective vaccine. The results obtained from this study confirmed that serological has a high sensitivity and specificity and are suitable for routine use, therefore Elisa techniques should be employed for routine use due to the high sensitivity and specificity of the techniques. This study recognized age, sex, vaccination, vitamine A intake and nutritional status of child, important demographic information.

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