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Serologic Evidence of Measles IgM Antibodies among Children in Two IDP Camps in Kaduna State, Nigeria

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Abstract
Major risk factors for the spread of measles in displaced populations are: poor vaccination coverage, mass migration causing international spread of diseases and high density of refugee population in the camps . The aim of this study was to determine the serologic evidence of measles IgM antibodies among children in two IDP camps (Ungwan zawu and Hayin Nariya) situated in Kaduna South and Kaduna North. Sample population consisted of 192 consenting children in the two IDP camps. About four (4) milliliters of blood was collected, dispensed into plain containers, allowed to clot and spun at 3,000rpm for 10 minutes. The serum was separated into cryo tubes and stored at -20^{0}C. The frozen sera were thawed at room temperature for 45 minutes and screened for measles IgM antibodies using ELISA technique (EuroImmun Medizinische Labordiagnostika AG, Germany) according to manufacturer's instructions. Measles specific IgM antibodies was detected in 66 (34.4%) of the total 192 children in the two IDP camps studied. Males recorded higher percentage prevalence of 63.6% compared to females (36.4%). Measles IgM antibodies varied among the age grades, from 63.6% in children aged >5years to 3.0% in children aged <1year. IDP Camp participants in Hayin Nariya camp recorded the highest measles IgM seropositivity of 75.8% than those residing in Ungwan Zawu (24.2%). Higher measles IgM antibody (51.5%) was found among participants with no history of previous vaccination (51.5%) compared to participants with history of vaccination (48.5%). Participants with previous history of measles attack recorded higher measles IgM antibodies (60.6%) than those without previous measles attack (39.4%). From the questionnaires administered, all the participants were exposed to crowd, all the mothers were illiterates and farming was their major occupation. Inadequate vaccination, malnutrition and lack of awareness are thought to be the reason for the high IgM antibodies. Measles awareness, and high vaccination coverage in IDP camps is advocated.

Keywords: IDP Camps, IgM antibodies, Measles, Overcrowding, Serologic Evidence

Introduction:

IDP Camps are erected sites with non-permanent shelters such as tents used for the collective and communal accommodation of evacuated or displaced persons. IDP camps can be planned for example purposely-built sites that is completed before or during influx or can be self-settled, that is, set up spontaneously by internally displaced persons or host communities without the support of the government or the humanitarian community (Kampala Convention, 2009). The United Nations High Commissioner for Refugees (UNHCR) states that as at April 2021 there have been an increased number of refugees and IDPs to 2.8 million owing to internal conflicts and natural disasters (UNHCR, 2021). The health care systems in these situations are often in a collapsed state or may become non-functional. Also, inadequate vaccination coverage, high concentration of displaced settlers and overcrowding in these camps are the ultimate causes of increased risk of infectious disease such as measles spread (Gayer *et al*., 2007).

Measles is a highly infectious disease caused by a paramyxo-virus belonging to the genus

Morbillivirus (Guerra *et al.,* 2017). Symptoms of measles disease include fever, cough, catarrh, inflammation of the conjunctiva and a generalized flat and raised, reddened erythematous rash (Biesbroeck and Sidbury, 2013). The virus route of transmission is the respiratory tract by aerosol spread or contact with fluids by either droplet from infected person's nose and mouth (WHO, 2014). The virus is known to cause disease only in humans and is highly contagious. Measles causes immunosuppression that persists for weeks to months after the acute infection. This may predispose infected individuals 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, infection of the upper airways and inflammation of the active tissues of the brain (encephalitis). Encephalitis is the most common cause of long-term sequelae and death (Perry and Haisey, 2004). Measles causes an estimated 1.4 million deaths annually, primarily in developing countries (Tulchinsky *et al.,* 1993).

Measles IgM antibodies are usually present in the blood of infected patients within 30days of onset of measles infection's rash. Measles infection is confirmed by laboratory isolation of measles IgM antibodies from blood samples of suspected cases. Moreso, measles IgM antibodies are raised in measles vaccinated patients as well as recently infected measles patients. Thus, the presence of measles IgM antibodies in children newly vaccinated with measles antigen within 30 days after vaccination, before blood sample collection and analysis does not mean measles disease (WHO, 2012). An outbreak of measles is confirmed by the laboratory when measles IgM antibodies have been seen in a patient's serum three consecutive times within 1month (Dubey and Choudhury, 2009).

Over the past few decades, the World Health Organization (WHO) has launched a number of programs in order to control and eliminate measles. Despite the great efforts, measles elimination could not be achieved especially in developing countries where there is massive population displacement. High measles associated death rates have been recorded in IDP camps as a major cause of child deaths in humanitarian emergencies (Tailey and Salama, 2003; Gayer *et al.*, 2007). Measles is a known cause of high morbidity and mortality mostly in children, especially in developing countries resulting in more than 95% measles-associated deaths (Bosan *et al*., 2002; Mohan *et al*., 2005). Measles is a public health concern among displaced persons owing to their characteristic massive population displacement, high level malnutrition, overcrowding in camps and inadequate measles vaccination coverage among the children (Kamugisha *et al.,* 2003). The case fatality rates in stable populations is approximately 2% but usually higher among populations displaced by disasters or other factors (Kouadio *et al*., 2010). There is paucity of data on serologic evidence of measles IgM antibodies among children in IDP Camps in Kaduna State, this therefore necessitated this study.

Materials and Method

Study Area

This research was carried out in two IDP camps located in Kaduna State, Northern Nigeria. The State has a land mass of 46,053 km^2 (17,781sq mi) and is drained by river Kaduna which defines the metropolis into Kaduna North and Kaduna South. The total land area of Kaduna State is 431km^2. It has a population of 6, 113, 503 million. The state is bordered by Zamfara State, Katsina State, Kano State and to the North West is Niger State.

Study Population

The study was carried out between December 2021 and February 2022. The sample population consisted of one hundred and ninety-two children below 5 years in two IDP camps (Ungwan zawu and Hayin Nariya) which are situated in Kaduna South and Kaduna North respectively.

Ethical Approval

Ethical approval for this research was obtained from the Ethics and research committee Ministry of Health, Kaduna State, Nigeria. Verbal informed consent was obtained from parents of the participating children before collecting their samples. A well-structured questionnaire was also administered to collect bio-data, socio-demographic information and medical history of each participant.

Sample Collection and Analysis
Venipuncture method of blood collection was used to obtain about four (4) milliliters of blood from the children using disposable syringe and needles. After collection, the samples were dispensed into sterile plain containers, allowed to clot, spun at 3,000rpm for 10minutes and the resultant serum was separated into cryo tubes and stored at -20^{0}C. The frozen sera were allowed to thaw at room temperature for about 45 minutes. The thawed sera were each screened for measles IgM antibodies using Enzyme Linked Immunosorbent Assay (ELISA) technique (EuroImmun Medizinische Labordiagnostika AG, Germany).

Each patient sample was analyzed according to manufacturer's instructions. Briefly, each patient sample was diluted 1:101 with sample buffer; that is 10ul sample to 1.0ml sample buffer, mixed well and incubated the mixture for at least 10min at room temperature. About 100ul of the calibrator, positive and negative controls and each diluted patient samples were transferred into the individual microplate wells according to the pipetting protocol and incubated for 30 minutes at room temperature (25^{0}C). The reagent wells were washed 3 times with 450ul working strength wash buffer. The wash buffer was left in each well for 30 to 60 seconds per washing cycle and emptied afterwards. After washing, the liquid was thoroughly disposed from the microplate by tapping it on absorbent paper with the openings facing downwards to remove all residual wash buffers. One hundred microliter (100ul) of enzyme conjugate (peroxidase labelled anti human IgM) was pipetted into each of the microplate wells. The preparation was incubated for 30 minutes at room temperature (Conjugation). The wells were emptied and washed. Thereafter, 100ul of chromogen/ substrate solution was pipetted into each of the microplate. It was incubated for 15 minutes at room temperature, protected from direct sunlight (Substrate incubation). Subsequently, 100ul of stop solution was pipetted into each of the microplate wells in the same order and at the same speed as the chromogen/substrate solution was introduced (Stopping the reaction). Photometric measurement of the color intensity was made at a wavelength of 450nm and a reference wavelength between 620nm and 650nm within 30 minutes of adding the stop solution.

Results Interpretation
The extinction value of the calibrator defines the upper limit of the reference range of non-infected persons (cut off) recommended by EUROIMMUN. Values above the indicated cut off are to be considered as positive while those below as negative.

Semiquantitative: Results can be evaluated semi quantitatively by calculating a ratio of the extinction value of the control or patient sample over the extinction value of the calibrator. The following formula was used to calculate the ratio:
Extinction of the control or patient sample: Extinction of calibrator
EUROIMMUN recommends interpreting results as follows: Ratio <0.8: negative; Ratio >0.8 to <1.1: borderline and Ratio >1.1: positive

Statistical Analysis
The descriptive statistics obtained from laboratory investigations was tabulated, encoded and statistically analyzed using Statistical Package for Social Sciences (SPSS) program. Chi square levels of significance were accepted at $p<0.05$.

Results
Measles specific IgM antibodies by ELISA was detected in 66 (34.4%) of the total 192 children in the two IDP camps studied (Table 1). Males recorded higher percentage prevalence of 63.6% to females 36.4%. This was statistically significant (P=0.023, OR=2.052, 95% CI=1.110-3.782) (Table 2).

Measles IgM antibodies varied among the age grades, from 63.6% in children aged >5years to 18.2% in children aged 3-4years to 15.2% in children aged 1-2years and 3.0% in children aged <1year (Table 2). Age grade significantly influenced the incidence of measles seropositivity among our study participants (P – 0.004, OR – 0.274, 95% CI – 0.06-1.36).

IDP Camp participants in Hayin Nariya camp recorded the highest measles IgM seropositivity of 75.8% when compared with their counterparts

residing in Ungwan Zawu which recorded 24.2%. This was statistically significant (P – 0.025, OR – 0.455, 95% CI – 0.242-0.869) (Table 3).

Measles IgM antibody seropositivity was higher among participants that had no history of previous vaccination (51.5%) when compared to participants that had history of previous vaccination (48.5%). Among the 48 cases that had previous history of measles attack, 60.6% were measles IgM antibodies seropositive while among the 144 cases that had no history of previous measles attack, 39.4% were measles IgM antibodies seropositive.

From the questionnaires administered, based on exposure to crowd as one of the risk factors for acquiring measles, all the children studied in the two IDP camps were exposed to crowd. All the mothers were illiterates and farming was their major occupation.

Table 1: Serologic Evidence of Measles IgM Antibodies among Children in Two IDP Camps in Kaduna State, Nigeria

Variable	No. Examined	Frequency	%	P-value	Odds Ratio	95% CI
Serology						
IgM Positive	192	66	34.4	<0.0001	0.274	0.179-0.421
IgM Negative	192	126	65.6			

Table 2: Serologic Evidence of Measles IgM Antibodies among Children in Two IDP Camps in Kaduna State, Nigeria in Relation to Gender and Age

Variable	Sample size	No Sero-positive	%age Seropositive	P-value	Odds Ratio	95%CI
Gender						
Males	100	42	63.6	0.0230	2.052	1.110-3.782
Female	92	24	36.4			
Age (Yrs)						
<1	10	02	3.0	0.004	0.274	0.06-1.36
1 - 2	38	10	15.2			
3- 4	56	12	18.2			
>5	88	42	63.6			

Table 3: Serologic Evidence of Measles IgM Antibodies among Children in Two IDP Camps in Kaduna State, Nigeria based on location of IDP Camp

Location of IDP Camp	Sample Size	No. Seropositive	% Seropositive	P-value	Odds Ratio	95%CI
Ungwan Zawu	68	16	24.2	0.025	0.455	0.242-0.869
Hayin Nariya	124	50	75.8			

Table 4: Serologic Evidence of Measles IgM Antibodies among Children in Two IDP Camps in Kaduna State, Nigeria based on previous history of vaccination status

Variable	Sample size	No Sero-positive	Percentage Seropositive
Vaccination Status			
Yes	144 (75.0)	32	48.5
No	48 25.0)	34	51.5
History of Measles Infection			
Yes	48 (25.0)	40	60.6
No	144 (75.0)	26	39.4

Discussion

The 34.4% measles IgM antibodies obtained in our study among children in the two IDP camps in Kaduna State, Nigeria is far lower than the 95% threshold level recommended by WHO (CDC, 2009). Measles susceptible individuals are children between 9 months to 15 years. The disease has endemicity in developing countries having highest peak of transmission from October (in the previous year) to March (the following year) (Guris, 2013). Factors influencing measles outbreaks are vaccine shortages and lack of proper storage systems (such as cold chain equipments) used to preserve the vaccines before they are sent (or before they get) to IDP camps and remote areas. Inadequate surveillance of measles case infections among IDP camp children and complete lack of awareness of what measles is all about among parents in IDP camps also contribute to measles outbreaks (Wolfson *et al*., 2009). Similar to our study, a total of 47,173 cases of suspected measles infected children were screened in some parts of Nigeria between January and July 2013 and a total of 34, 963 tested positive for measles IgM antibodies (CDC, 2013).

Our study recorded a significantly higher percentage of males having measles IgM antibodies than females. Similarly, a study on measles outbreak in South-western parts of Nigeria recorded higher measles infection among males than females (Adeoye *et al*., 2010; Isere *et al*., 2015). Our study populations were majorly children between the ages five years and below. Measles IgM antibodies varied among these age grades, from 63.6% in children aged >5years to 3.0% in children aged <1year. Age had a statistically significant influence on the incidence of measles IgM seropositivity in our study. Our findings are in agreement with reports on measles outbreaks in various regions: 89% in Osun State, Nigeria; 24.3% in Delma district, Nigeria and 73% in Maroua, Cameroon where the highest prevalence of measles infection was observed in children between five years and below (Fatiregun *et al*., 2009; Pradeep *et al*., 2012; Goodson *et al*., 2011).

IDP Camp participants in Hayin Nariya camp recorded a significantly higher measles IgM seropositivity of 75.8% when compared with their counterparts residing in Ungwan Zawu (24.2%). Crowded and clustered conditions of the settlement pattern of the houses and settlers in the Hayin Nariya camp might be the reason for this higher IgM antibody. Higher measles IgM antibody seropositivity (51.5%) was found among participants that had no history of previous measles vaccination while 48.5%

measles IgM antibodies was found among previously vaccinated participants. The resultant high percentages of unvaccinated population recorded in our study were similar to findings in previous reports on measles outbreaks in some parts of Nigeria and some developing countries (Fetuga *et al*., 2007; Fatiregun *et al*., 2009). An inference drawn from this is that there is probably low vaccination coverage of these IDP camp children as well as lack of awareness on the importance of measles vaccine among the parents .With the 60.6% measles IgM antibodies obtained from participants that had history of previous attack of measles infection and the 39.4% measles IgM antibodies obtained from participants that had no history of previous attack of measles infection; It cannot be overemphasized the need for high measles immunity in order to limit or prevent a possible outbreak of measles disease among these IDP camp children. This is because they are continually exposed to crowds due to their daily activities**.** The high measles immunity needed to prevent an outbreak can only be gotten through a large vaccination program in these IDP camps as well enlightenments of their parents (Mohan *et al.,* 2005; Fetuga *et al*., 2007; Fatiregun *et al*., 2009; CDC, 2009).

From the questionnaires administered, all the participants were exposed to crowd. All the mothers were illiterate and farming was the major occupation. Despite the probable availability of health facilities that provides routine immunization to measles, a large number of these IDP parents do not utilize them. Thus, the severity of measles epidemic is more in the Northern part of Nigeria than the Southern part of Nigeria due to illiteracy, lack of awareness, unavailability of vaccines in IDP camps (owing to shortages), logistic problems, lack of mobile transportation mediums to get these vaccines to these IDP camps and low socio-economic status of the IDP camp parents (Fetuga *et al*., 2007; Dubey and Choudhury, 2009).

Conclusion

*S*erologic evidence of measles IgM antibodies was *34.4%. Sex, age and location of IDP camps significantly influenced the serological evidence of measles IgM antibodies among our study population*. Measles awareness, high vaccination coverage in IDP camps and enlightenment of displaced mothers on the danger associated with measles infection and outbreak is advocated.

Study limitations

A limitation is the small sample size in this investigation orchestrated by financial constraint.

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Authors Contributions

Moses-Otutu Ifueko Mercy designed the study and drafted the manuscripts. All authors carried out data and sample collection, organization and laboratory investigation. Anene Chioma Precious conducted literature search while all authors read and approved the final draft.

Conflicts of Interest

The authors attest that they all agree to the entire research and that there are no conflicting interests in this research

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