



Original Article:

The Impact of Immunization Control Activities on Measles Outbreaks in Akwa Ibom State, South-South, Nigeria

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Abstract:

Background: The increase of vaccination rates means that fewer children will be vulnerable to vaccine preventable diseases such as measles, which will invariably result in a drop in the infant mortality and morbidity rates. **Objective:** To assess the impact of the implementation of measles reduction strategies from 2006 to 2008 using the quarterly national program for immunization (NPI) in Akwa Ibom state, Nigeria. **Method:** Following informed consent, individuals presenting with febrile rash illnesses were routinely bled and tested for measles specific IgM using commercially available ELISA kit-MV-ELISA (Enzygnost; Behring Diagnostics, Marburg, Germany) in accordance with the manufacturer's instructions. **Results:** A total of four hundred and four individuals comprising of 216 vaccinated and 188 unvaccinated, presenting with febrile rash illness were screened for measles specific IgM antibodies as indication of active infection between January 2006 and December 2008 out of which 122 (30.2%) had detectable levels of measles antibodies. Among the vaccinated and unvaccinated groups, 32 (14.8%) and 90 (47.9%) respectively were detected with measles IgM antibodies. The highest and lowest antibody levels were detected in 2006 (vaccinated: 54.7%; unvaccinated: 78.4%) and 2008 (vaccinated: 1.2%; unvaccinated: 12%) respectively. The distribution of measles burden by year show an overall decline in prevalence from 70% in 2006, 8.9% in 2007 to 3.7% in 2008. While, children under the age of 5 similarly had a decline in measles incidence of 73.3%, 10.7% and 3.3% respectively. Sex distribution of infection within the 3-year period shows that more females (37.4%) than males (21.2%) expressed measles IgM antibodies, and active infection was detected more in the rural (31.4%) than urban area (27.7%). However, findings indicate a tremendous decline in active infection in the rural areas from 67% in 2006 to 0% in 2008, and in the urban areas from 78% in 2006 to 9.3% in 2008 among both vaccinated and unvaccinated groups. A highly significant reduction in measles infection was observed more among males than females ($P=0.009$). Infection distribution by location did not show any significant difference ($P=0.65$) even though more individuals in the rural areas were noted with active infection. **Conclusion:** The study shows a highly significant reduction in measles burden among vaccinated individuals ($P=0.0001$) and invariably increases protective coverage of measles vaccination most especially among children under 5 years of age ($P=0.0066$) in the state. Findings justify effort by government and WHO in carrying

immunization campaigns in children, 5-years and below irrespective of vaccination status and experience. **Key Words:** Measles vaccination, measles-specific IgM, Akwa Ibom state

Introduction:

The World Health Organization estimates that almost one million measles related death occurs every year, majority (85%) in Africa and Asia.(1) In Nigeria, measles remains a major cause of childhood morbidity and mortality despite the introduction of safe and effective vaccines since 1963. An estimated 750,000 measles deaths has been reported to have occurred worldwide in 2000.

In 2005, the WHO and partners made a commitment to reduce measles morbidity in poor resource settings by 90% by the end of the first decade of the millennium.(1) This commitment was reaffirmed by member states at the 2008 assembly. The reasons for seeking to control measles outbreaks in poor resource settings are as compelling as those in industrialized nations. Infants in developing countries are more likely to receive measles vaccine under suboptimal conditions, and with significantly lower efficacy than in industrialized countries. Subsequently, the number of individuals susceptible to measles accumulates rapidly, leading to more frequent occurrence of epidemics affecting mostly younger children, even in settings where immunization coverage is relatively high. The combination of these and other factors such as crowding, malnutrition and lack of supportive care may result in substantial outbreak morbidity in developing countries, with case fatality rates that are frequently over 10%.(2) The WHO strategy is to reduce measles mortality targets to achieve more than 90% routine immunization coverage before the first birth day of a child. The strategy also emphasizes efforts to ensure that all children have a second chance for measles vaccination during the second routine dose or supplemental immunization activities. The other strategy comprises of effective laboratory-supported surveillance and provision of appropriate clinical management for measles cases.(3,4)

Following the worldwide implementation of these immunization strategies, it was observed that the number of reported measles cases had cumulatively decreased from 852,937 in 2000 to 279,006 in 2007. Indeed all WHO regions reported a decline in measles cases, but the largest occurred in the Americas (93%) followed by African regions (85%), while the

smallest decline of 12% occurred in the South-East Asian Region.(5)

In this study, we assess the impact of the implementation of measles reduction strategies among the younger and older children between 2006 and 2008 in Akwa Ibom state in line with WHO and partners' strategic objectives.

Materials and Methods:

Study population

This study was conducted between January 2006 and December 2008 among individuals presenting with febrile rash illness in 324 health care facilities spread across Akwa Ibom state. These health facilities were 296 primary and 28 secondary health care facilities that serve the inhabitants of the state. A total of 404 patients were recruited for the study. The Blood specimens were obtained between the first and 7 days of rash onset. Convalescent-phase specimens were collected approximately two to three weeks after onset of rash. The mean age of subjects was 11.5 years \pm 5.91 SD; males were 193 and female 211.

Sample collection

Five (5) ml of blood was collected from each subject into plain sterile bottle following informed consent. Blood samples were centrifuged and sera was separated and stored at -20°C until used. Samples were analyzed in batches for measles specific IgM using commercial ELISA (MV-ELISA) (Enzygnost; Behring Diagnostics, Marburg, Germany) in accordance with the manufacturer's instructions. Tests were read on a pre-programmed spectrophotometer Quantum II, wavelength 450/630nm, manufactured by Abbott.

Statistical Analysis

Results were presented on frequency tables by year. The comparison of characteristics of subjects by year was carried out

using Graph Pad Prime version 5.3 statistical package at 95% Confidence Interval (CI). The level of statistical significance was established at $p = 0.05$ using Fisher's exact 2-tailed values.

Ethical Issues:

Appropriate informed consent and ethical approval were obtained from the subjects and authorities of the health institutions respectively.

Results:

A total of four hundred and four (404) blood specimens taken from individuals with febrile rash illness seen in health facilities across Akwa Ibom state were tested and analysed for measles specific IgM antibodies to indicate those with active infection. Increase in routine measles vaccination resulted in decrease in number of measles specific IgM positive cases seen (Fig. 1).

Table 1 indicates Prevalence of measles antibodies in individuals with febrile rash illness in 2006. The highest prevalence of 73.3% infections occurred in those under 5 years of age, those in age group 6-10 years recorded 42% and those aged 11-15 years recorded 33%. None of the individuals in the age bracket 16-20 years and above had measles infection. Findings from this study show that individuals who did not receive at least one dose of measles vaccination in 2006 had the highest prevalence of 74%, while those who received at least one dose of vaccination had a prevalence of 55%. Females (87%) were more susceptible for measles than males (52%). Examining infection by location revealed that urban dwellers (78%) were more susceptible than rural dweller (67%). However, there was no statistically significant difference in the occurrence of measles cases between age groups, age, sex, vaccination status and by location ($P > 0.05$).

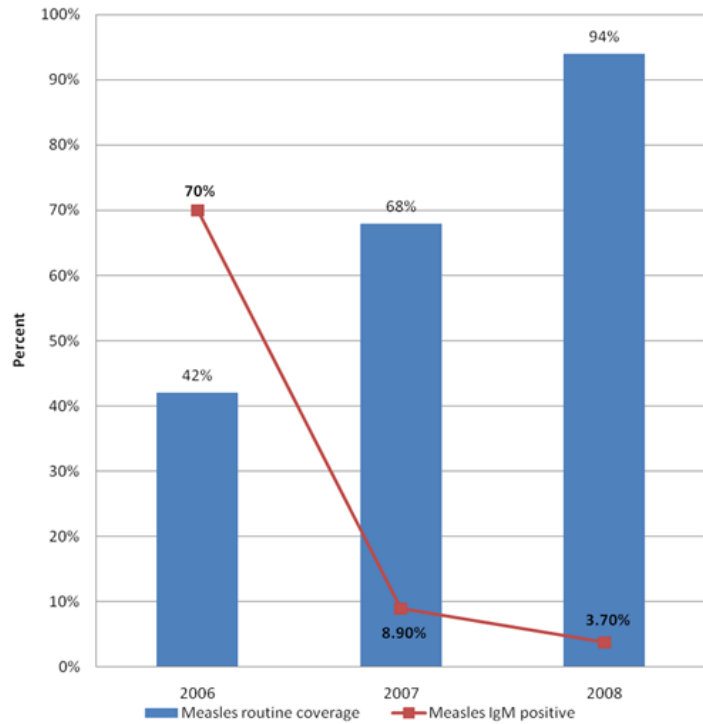


Fig.1: Prevalence of measles IgM against routine measles vaccination coverage

Table 1: Prevalence of measles antibodies in individuals with febrile rash illness, 2006

Characteristics	Number screened	Number positive	Percentage Positive	P-value
Age (years):				
0 - 5	135	99	73.3%	0.4451
5-10	12	5	42.0%	
10-15	3	1	33.0%	
15-20	0	0	0.0%	
20+	0	0	0.0%	
Vaccination status:				
Vaccinated	53	29	55%	0.22
Un-vaccinated	97	76	74%	
Sex:				
Male	72	37	52%	0.12
Female	88	68	87%	
Settings:				
Rural	109	73	67%	0.6
Urban	41	32	78%	

Findings among subjects studied in 2007 show that a 7-fold decline in measles burden among children under 5 years of age (10.7%), followed by those aged 6-10 years (7.1%). As observed in 2006, none of the individuals in the age bracket 16-20 years and above had measles infection. Similarly, females (10.8%) were more infected than males (5.6%), while none of the subjects in the urban areas had measles IgM antibodies unlike those in rural setting that recorded 13% prevalence. Measles prevalence among the vaccinated subjects declined to 2.5% as against 16.7% among the unvaccinated (Table 2).

Table 2: Prevalence of measles antibodies in individuals with febrile rash illness, 2007

Characteristics	Number screened	Number positive	Percentage Positive	P-value
Age (years):				
0- 5	103	11	10.7%	1.000
5-10	28	2	7.1%	
10-15	14	0	0.0%	
15-20	0	0	0.0%	
20+	1	0	0.0%	
Vaccination status:				
Vaccinated	80	2	2.5%	0.008
Un-vaccinated	66	11	16.7%	
Sex:				
Male	71	4	5.6%	0.361
Female	65	7	10.8%	
Settings:				
Rural	100	13	13%	0.021
Urban	46	0	0.0%	

In 2008, measles prevalence among 0-5 years old further declined to 3.3%, more than 3-fold the prevalence of previous year while, absence of measles infection was observed among children in the lower age group of 11 years and above. As observed in the previous 2 years, infections among the un-vaccinated subjects were higher than the vaccinated (12% vs. 1.2%), while none of the males tested had measles unlike the females where (6.9%) had positive IgM antibodies. A converse situation was reported among those in the urban locations where 9.3% prevalence was recorded as against none among those in the rural areas (Table 3).

Table 3: Prevalence of measles antibodies in individuals with febrile rash illness, 2008

Characteristics	Number screened	Number positive	Percentage Positive	P-value
Age (years):				
0- 5	91	3	3.3%	0.3861
5-10	11	1	9.1%	
10-15	5	0	0.0%	
15-20	0	0	0.0%	
21+	1	0	0.0%	
Vaccination status:				
Vaccinated	83	1	1.2%	0.047
Un-vaccinated	25	3	12%	
Sex:				
Male	50	0	0.0%	0.126
Female	58	4	6.9%	
Settings:				
Rural	65	0	0.0%	0.028
Urban	43	4	9.3%	

Table 4 illustrates the cumulative measles prevalence in individuals with febrile rash illness. Cumulatively, children under 5 years of age were most infected with measles, 34.3% within the 3-year period, while those aged 6-10, and 11-15 years recorded 13.7% and 4.8% respectively. None of the older children suffered measles infection. There was significant difference in the prevalence of measles between the age groups considered ($\chi^2 = 10.03$, $P = 0.0066$).

Table 4: Cumulative prevalence of measles antibodies in individuals with febrile rash illness

Characteristics	Number screened	Number positive	Percentage Positive	P-value
Age (years):				
0- 5	329	113	34.3%	0.0066
5-10	51	7	13.7%	
10-15	22	1	4.5%	
15-20	0	0	0.0%	
21+	2	0	0.0%	
Vaccination status:				
Vaccinated	216	32	14.8%	0.0001
Un-vaccinated	188	90	47.9%	
Sex:				
Male	193	41	21.2%	0.0090
Female	211	79	37.4%	
Settings:				
Rural	274	86	31.4%	0.6568
Urban	130	36	27.7%	

Fig. 1 shows routine annual measles immunization coverage and prevalence of measles in both children vaccinated and unvaccinated in Akwa Ibom state. It was clear that increases in measles immunization coverage proportionately cause a decline in measles prevalence among children in the state. Yearly distribution of presence of measles IgM antibodies in children shows that a drastic decline in measles prevalence from 70% in 2006 to 3.7% in 2008. Children under the age of 5 similarly had a decline in measles incidence of 73.3%, 10.7% and 3.3% in 2006, 2007 and 2008 respectively. A highly significant association between development of measles and vaccination status of children was also observed in this study ($P=0.0001$) with measles prevalence among the vaccinated being 14.8% as against 47.9% prevalence among the unvaccinated subjects. Measles cases were higher among rural dwellers than the urban dwellers (31.4% vs. 27.7%). However, there was no statistically significant difference in the occurrence of measles cases between at the two settings ($P=0.6568$). In respect of gender, a cumulative measles prevalence of 37.4% was reported among females, while 21.2% was reported males ($P=0.009$).

Discussion:

Two-third of pregnant women in sub-Saharan Africa attend ante-natal clinic at least once during pregnancy, an opportunity to provide them with health education, counselling, tetanus toxoid and information on the benefits of presenting their wards for routine immunization after birth.[6] Measles outbreaks have continued to occur in highly immunized populations due to efficient transmission of the virus among susceptible individuals.[7] This study aimed to evaluate the impact of measles immunization control activities on measles outbreaks in poor resource settings.

Findings show that the prevalence of measles varied considerably between age groups, vaccination status, sex and community settings. The study revealed that 122 (30.2%) of the 404 individuals screened had detectable levels of measles specific IgM antibodies in their blood. This finding is slightly lower than the 32% reported in Ilorin, North Central Nigeria (8), much lower than 55% recorded in a study conducted in Lagos (9) but higher than 15.6% reported in another study in Southwestern Nigeria.(10) Elsewhere in Africa, 73.7% has been reported in Ghana (11) and 86.1% in Alexandria, Egypt. (12) The reason for the observed differences may be attributed to the seriousness and dedication of relevant authorities in ensuring a better measles vaccination coverage in their domain.

From the results of this study, the proportion of the population with detectable measles IgM antibodies, indicating active infection, declines rapidly between within the 3 year period of study. This positive development could be attributed to the sustained effort toward increase in routine immunization cov-

erage in the state. Measles incidence declined from 70% in 2006, to 8.9% in 2007 and later to 3.7% in 2008. These data show that measles incidence decreases as vaccination coverage increases from 42% in 2006, 68% in 2007 and 94% in 2008. In this study, the proportion of measles cases recorded in children aged 5 years and below was lower than that reported by Opaleye et al. (13) in southwestern Nigeria (34.3% vs 46.5%). Similarly, another study in Lagos, southwestern Nigeria also reported a higher measles prevalence (55%) among this age group of children.(9) The age-specific incidence indicates that children under 5 years of age in Akwa Ibom state and Nigeria in general were at a higher risk of contracting measles compared to older children. However, this is inconsistent with report from other part of the world such as Saudi Arabia children at higher risk are those within the age bracket of 5-15 years old.(14) This study also reveals that positive cases of measles decreases as the age of children increased. This trend may be attributed to physiological status of the individuals and variation in prevailing environmental factors.(1) In addition, immunity acquired by older children over the years as a result of sub-clinical infections might provide the required protection against measles.(4)

In this study, female population were seen to be more susceptible to measles than male counterpart. This is in consonance with the report by which documented that measles antibodies is marginally higher in females than males. (15)

The overall prevalence of measles in this study shows a significantly higher infection rate (47.9%) among the unvaccinated populations compared to 14.8% observed among the vaccinated populations, including those who had received at least one dose of measles vaccine through routine immunization. The incidence of measles among the vaccinated group, (which those who received at least one dose of measles vaccine) in this study was 2-fold less than that reported in Alexandria, Egypt.(16)

Cases of measles seen in subset of individual who did not undergo serological conversion after vaccination is known as primary vaccine failure.(17) The limitation in correctly evaluating primary vaccine failure could be as a result of variation in sample size, method of verification of vaccination status, age at the time of vaccination, number of doses, immunogenicity of the strain of the virus used to manufacture the vaccine, improper handling/storage of the vaccine. (18) However, in this study, the 14.8% of vaccinated individuals detected with measles IgM antibodies, indicating active infection, may said to be experiencing vaccine failure. The concern of these findings is the fact that the rate of failure is higher than the acceptable rate for measles vaccination failure stipulated in the range of 2 to 10%.(19)

Findings in this study further reveal a higher percentage of measles IgM antibody positivity among those living in rural areas than in urban settings. This is inconsistent with previous study that reported high measles IgM positivity among urban dwellers (20), and another which reported that measles is a more common health problem in urban dwellings.(12) The variation in serologic profile between urban and rural settings might be due to malnutrition, overcrowding and inadequate or lack of supportive health care in rural communities, the children might also receive vaccine of low potency, due interruption in the cold chain system, frequent booster of natural measles in urban areas with population densities.(20)

This study is relevant in the global measles elimination initiative. No such studies have been carried out in Akwa Ibom state; therefore, this study provides baseline information for potential interventions in the state. The fact that there was overall drastic reduction in measles burden from 70% in 2006, to 3.7% in 2008 testifies to a favourable measles vaccination impact in the state and further support effort by government and WHO to conduct mass measles vaccination across children, 5 years and below irrespective of previous vaccination experience/status.

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