

Immunoglobulin M (IgM) Positivity among Suspected Measles Cases in Under-Five Children in South West Nigeria

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Abstract

Worldwide, Measles is fifth leading cause of death among Under-five children. This study analyzed the Immunoglobulin M (IgM) positivity and compared it with the immunization status among suspected measles cases. A descriptive cross-sectional study was carried out using records of all the 2375 suspected measles cases reported under the Integrated Disease Surveillance and Response to the World Health Organization Laboratory in Nigeria in year 2011. Frequency tables and cross tabulations were generated and p-value of less than 0.05 was significant. Analysis was done using SPSS. There were 2375 suspected measles cases (7 per 100,000 population) out of which 1552 (65%) were Under 5 children (22 per 100,000 Under 5 population). Those that were laboratory confirmed IgM positive cases were 602 (38.7%) which corresponds to 9 per 100,000 Under 5 population. Of those who were IgM positive, 139 (23.1%) were vaccinated before the onset of symptoms. However amongst those that were IgM negative, 357 (39.6%) had a history of vaccination before onset of symptoms. Findings are suggestive of vaccine failure and missing of immunization. There is therefore the need to intensify measles immunization campaigns and introduce a second dose to enhance the goal of eliminating Measles.

Keywords: Immunoglobulin, Measles, Under-five.

Introduction

Measles is a highly contagious viral disease associated with high morbidity and mortality. In the pre-vaccine era an estimated 130 million cases occurred each year.¹ Despite efforts put towards its elimination by the World Health Organization (WHO) and United Nations Children's Fund (UNICEF), measles has remained a public health challenge with an estimated 139,000 measles deaths occurring globally in 2010 – mostly children under the age of five.² Measles is a leading cause of childhood mortality globally. Studies have shown that infants had two-fold higher case death than older measles cases.³ In 2005 an estimated 242,000 children died worldwide from measles.⁴

Measles infection is still largely endemic in many developing countries of Africa and South Asia, including Nigeria, with periodic outbreaks despite efforts to achieve elimination goals.⁵⁻⁸ Also most measles deaths occur in these regions.⁴ More than 95% of measles deaths occurred in developing countries.² Member states of the World Health Organization (WHO) African regions (AFRO) have therefore set goals for measles elimination by 2020.⁹ One of the key components of the WHO/UNICEF Global Plan for Measles Mortality Reduction, 2006-2010 strategic plan is to provide the first dose of measles vaccine to successive groups of all children at the age of nine months or shortly after especially in countries with high measles burden.¹ Two doses of vaccine are recommended as about 15% of vaccinated children fail to develop immunity from the first dose.²

High vaccination coverage especially in children by age 2 years has resulted in low levels of most vaccine-preventable diseases.¹⁰ Though a significant decrease in the incidence of measles has been achieved, more effort is needed to reach the goal of eliminating the disease in all the WHO regions as frequent outbreaks still occur. Outbreaks have recently been reported in some countries including southeastern France (January to June 2003),¹¹ South Africa (2009-2010),¹² China (2005-2010),¹³ Ethiopia, Kenya, and Somalia (2010-2011),⁹ and the region of Dakar in Senegal (2009).¹⁴ Children under 5 accounted for 67.4 % of the total number of cases in Dakar.¹⁴ Most of these measles outbreaks has been linked to low vaccination coverage^{9,11} and most cases occurring predominantly in unvaccinated individuals.^{7-9,14} To further reduce the burden of disease and prevent outbreaks, vaccination coverage must be improved on particularly in populations with lower vaccination coverage.

The diagnosis of many viral diseases has historically relied on the detection of antibodies in serum or plasma.^{15,16} Measles IgM antibodies are markers of recent infection or vaccination.⁷ Measles-specific immunoglobulin M (IgM) and immunoglobulin G (IgG) are both produced during the primary immune response and can be detected in the serum within a few days of rash onset, using a sensitive enzyme-linked immunosorbent assay (EIA). IgM levels peak after 7–10 days of rash onset and then decline, being rarely detectable after 6–8 weeks.¹⁷ The detection of measles-specific immunoglobulin M (IgM) has become a standard diagnostic method for the laboratory confirmation of measles infection.^{1,17} WHO recommends IgM antibody detection by ELISA as the standard test for routine measles surveillance.^{1,4} This aim of this study is to assess IgM immunopositivity among suspected measles cases in children under-five in South-western Nigeria, and its association with immunization status and timing of immunization.

Methodology

Laboratory records of suspected Measles cases reported as part of the measles surveillance program, to the World Health Organization (WHO) Offices in the South Western region of Nigeria between Jan 2011 and December 2011 were retrospectively reviewed. Basic demographic information, date of onset of symptoms, date of last vaccination, age at vaccination, and Immunoglobulin M (IgM) results of the 1552 suspected cases among children under-five reported were analyzed.

The presence of measles-specific Immunoglobulin was tested in the Measles Laboratory using EIA serological tests for detecting IgM antibodies according to the WHO recommendations.²² Records of patients with incomplete data were excluded from the study. SPSS version 15.0 was used to analyse the data. An analysis of immunization status and timing of immunization as well as their association with immunoglobulin positivity was done. Yates Chi-square test was used to estimate the statistical differences between IgM result compared with immunization status on one hand and with cases with immunization greater than two months to onset of symptoms on the other hand. A p-value of less than 0.05 was considered as statistically significant.

A suspected case of Measles is a patient with generalized maculo-papular rash, fever and either of cough, coryza and conjunctivitis. Laboratory diagnosis was taken as presence of measles-specific IgM antibodies.

Results

The proportion of those under the age of five among measles cases is 65.0%. Among the suspected measles cases under the age of 5, more (53.0%) were males while 47.0% were females. Some (32.6%) of them were vaccinated against measles, 28.0% were unvaccinated while many of the cases (64.6%) were not sure whether they were vaccinated or not before onset of symptoms. Also, 12.2% were vaccinated less than 2 months before the onset of symptoms and 23.2% were vaccinated more than two months before symptoms started. Out of all the cases of measles, a little more than half (58.0%) had negative IgM result while 38.7%, 1.0% and 2.2% had positive, intermediate and unknown IgM results respectively.

Most (73.3%) of the cases with positive IgM results were unsure of vaccination while 23.05 and 3.7% of them were vaccinated respectively. The cases with negative IgM results had 58.0%, 39.6% and 2.4% of them unsure of vaccination, vaccinated and unvaccinated respectively. As for the timing of measles vaccination and onset of symptoms of measles, 11.5% and 15.3% of the cases with positive IgM had their vaccination less than 2 months and greater than two months respectively before the onset of symptoms. Also, 13.1% and 28.9% of

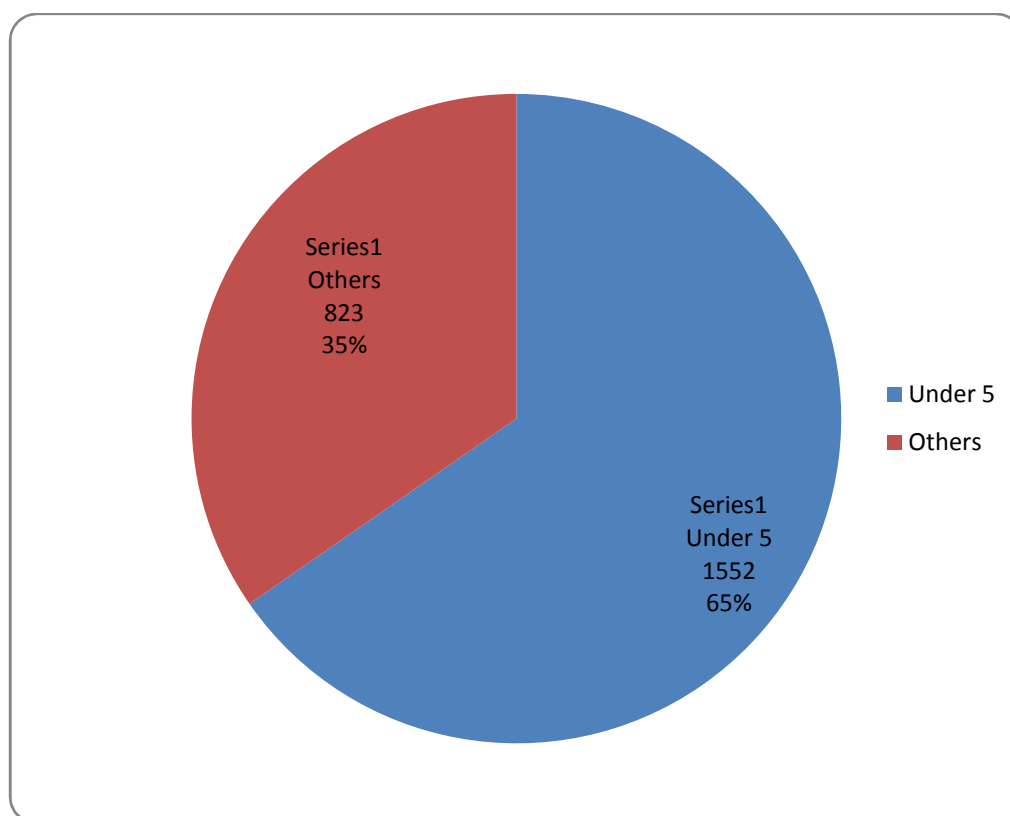
those with negative IgM had measles vaccine less than 2 months and greater than two months respectively before onset of symptoms.

Discussion

In this study, laboratory records of 1552 suspected measles cases reported as part of the World Health Organization (WHO) measles surveillance program in Nigeria between January 2011 and December 2011 were reviewed and basic demographic information, date of onset of symptoms, date of last vaccination, age at vaccination, and Immunoglobulin M (IgM) results of the 1552 suspected cases among children under-five reported were analyzed. Most of those affected by measles were those under the age of 5. This is in keeping with a study carried out in Dakar, Senegal¹⁴ in which 67.4% of the measles cases were under 5 and also with findings in a research paper on measles outbreak investigation in Southwest Nigeria.⁷ Also, the analysis of measles case-based surveillance in Nigeria between 2006 and 2009 revealed that most confirmed cases of measles were among children under 5 years of age.⁸ Among the suspected measles cases under the age of 5, more (53.0%) were males while 47.0% were females. Some (32.6%) of them were vaccinated against measles, 28.0% were unvaccinated while many of the cases (64.6%) were not sure whether they were vaccinated or not before onset of symptoms. This is not what would be expected as the circulation of the measles virus usually reflects low vaccination coverage.¹¹ It is probable that most of the 64.6% in this study whose vaccination was unsure before they had measles were actually unvaccinated. Other previous studies also suggested that measles cases occurred predominantly in unvaccinated persons^{8,9} and regions with lowest routine immunization coverage had the highest number of measles morbidity and mortality.⁸

Majority (73.3%) of the cases with positive IgM results were unsure of vaccination while 23.05 and 3.7% of them were vaccinated respectively. The cases with negative IgM results had 58.0%, 39.6% and 2.4% of them unsure of vaccination, vaccinated and unvaccinated respectively. While a little more than half (58.0%) of the measles cases had negative IgM result, 38.7%, 1.0% and 2.2% had positive, intermediate and unknown IgM results respectively. This is against what is expected. As much as 71% of suspected measles cases had positive IgM in samples collected on the first day of disease and up to 88% had positive IgM at 4 weeks after onset of measles symptoms in one previous study¹⁵ while another study even reported a 73.0% IgM positivity rate as low.¹⁷ The process and timing of sample collection, handling of samples as well as testing conditions may need to be evaluated to make necessary amendments where lapses are noticed in order to improve quality of assay and IgM positivity results in measles cases.

There is high proportion of children that were not vaccinated among those who were IgM positive. There is also significant proportion of those who had a history of having received measles vaccine yet were IgM positive; this is suggestive of vaccine failure. It is therefore important to intensify measles immunization campaigns to cover those that are not yet vaccinated. It is also important to introduce a second dose of measles vaccine to ensure that the children who did not receive the first dose are covered and to also address primary vaccine failure among those who were initially vaccinated. It is expected that these will enhance the goal of eliminating measles.

Tables and Figures:**Figure 1:** Proportion of Under-five among suspected measles cases**Table 1:** Demographic information of suspected measles cases among 0 – 59 months

Variable	Frequency	Percent
Sex		
Male	823	53.0
Female	731	47.0
Immunization status before onset of symptoms		
Vaccinated	506	32.6
Unvaccinated	44	2.8
Unsure	1004	64.6
Timing of immunization		
< 2 mths	190	12.2
> 2mths	360	23.2
Unsure	1004	64.6
Province		
Ekiti	172	11.1

Lagos	444	28.6
Ogun	321	20.7
Ondo	129	8.3
Osun	144	9.3
Oyo	344	22.1

Table 2: Immunoglobulin results for measles samples

Variable	Frequency	Percent
Measles IgM result		
Positive	602	38.7
Negative	902	58.0
Intermediate	16	1.0
Unknown	34	2.2
Rubella Igm Result		
Positive	76	4.9
Negative	448	28.8
Intermediate	33	2.1
Not Done	580	37.3
Unknown	417	26.8

Table 3: Measles IgM result with Immunization status before onset of symptoms and timing of Immunization

Variables	Frequency (percentage)				χ^2	P _{value}
	Positive	Negative	Intermediate	Unknown		
Immunization status before onset of symptoms						
Vaccinated	139 (23.1)	357 (39.6)	4 (25.0)	6 (17.6)	51.200	0.000

Unvaccinated	22 (3.7)	22 (92.4)	0 (0.0)	0 (0.0)
Unsure	441 (73.3)	523 (58.0)	12 (75.0)	28 (82.4)

Timing of Immunization

< 2months	69 (11.5)	118 (13.1)	1 (4.2)	2 (5.9)	48.591	0.000
> 2 months	92 (15.3)	261 (28.9)	3 (18.8)	4 (11.8)		
Unsure	441 (73.3)	523 (58.0)	12 (75.0)	28 (82.4)		

Table 4: Rubella Igm with Immunization status before onset of symptoms and Timing of Immunization

Variables	Frequency (percentage)					χ^2	P _{value}
	Positive	Negative	Intermediate	Not Done	Unknown		
Immunization status before onset of symptoms							
Vaccinated	36 (47.4)	183 (40.8)	18 (54.5)	133 (22.9)	136 (32.6)	56.815	0.000
Unvaccinated	0 (0.0)	13 (2.9)	0 (0.0)	22 (3.8)	9 (2.2)		
Unsure	40 (52.6)	252 (56.3)	15 (45.5)	425 (73.3)	272 (65.2)		
Timing of Immunization							
< 2months	16 (21.1)	73 (16.3)	6 (18.2)	68 (11.7)	27 (6.5)	66.241	0.000
> 2 months	20 (26.3)	123 (27.5)	12 (36.4)	87 (15.0)	118 (28.3)		
Unsure	40 (52.6)	252 (56.3)	15 (45.5)	425 (73.3)	272 (65.2)		

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