Low Level of Pre-Vaccination Measles Antibody among Infants Receiving Measles Immunization in Ilorin, Kwara State, Nigeria

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Abstract   This study was designed to assess the low levels of pre-vaccination measles antibody among infants receiving measles immunization in Ilorin, Kwara State, Nigeria. Pre-vaccination blood samples were obtained from 400 infants brought to the EPI Clinic of the University of Ilorin Teaching Hospital, Ilorin, Nigeria. Blood samples were collected by finger puncture onto ROPACO (Rochester, USA) rectangular filter paper measuring 7 cm by 10 cm. Other information like name, age, sex, date of vaccination was also recorded on the filter paper. The filter papers were dried at ambient temperature and stored in plastic bags at -20℃ until ready for serum extraction. Specimens were analyzed for measles antibody using Hemagglutination Inhibition technique. Data generated were subjected to Chi square statistical test to establish association between categorical variables with dichotomous outcomes. Of all the 400 infants screened for pre-vaccination measles antibodies, 29(7.2%) had protective antibody titer while 156 (39.0%) had low titer since ≥40 HI titer is the study threshold of protection against measles while 215(53.8%) had no detectable measles antibody titer (<1:10). Thirty-one (8.0%) of the infants had measles prior to vaccination. Previous history of measles was significant associated (P=0.0005, X2 = 34.507) with the level of pre-vaccination measles virus antibody. There was no significant difference (p=0.723) in the level of measles virus antibody among the exclusively breastfed infants and those that were not exclusively breast fed. Age (p=0.839) and sex (p=0.1999) were not significantly associated with the level of measles virus antibody. The distribution of this antibody levels appeared stable with no significant difference between age groups, sex and breast feeding pattern. Only the previous history of measles showed statistical association with measles virus antibody proportion. In conclusion, a larger proportion (53.8%) of the children had no detectable anti-measles virus antibody while 39.0% had low (non-protective) titer; these put both groups at risk of developing measles given the endemic nature of Nigeria. Therefore, re-evaluation of 9 months as the age for measles vaccination in Nigeria vis-à-vis 92.8% with <40 HI titer is highly recommended.

Keywords   Hemagglutination Inhibition, Pre-vaccination, Measles Antibody, Measles Immunization, Vaccination

1. Introduction

Measles infection occurs worldwide but it is epidemic in developing countries where severe morbidity and high mortality are associated with underlying malnutrition, poverty, and indiscriminate vaccination services[1- 3]. The optimum age for measles vaccination varies from country to country thus a standardized vaccination schedule is controversial. While the increase in measles vaccination coverage has produced significant changes in the epidemiology of infection in developing countries, measles morbidity and mortality represents an important public health problem, with a significant number of infections occurring earlier than the 9 months[4]. Several researchers have reported the occurrence of measles in infants less than 9 months old[5-6]. Some studies have attributed the occurrence of measles among infants less than 9 months to low affinity maternal measles antibody which consequently increases the vulnerability of these infants to circulating wild measles strains[7-8]. Oyedele et al.[6] revealed that while 58% of Nigerian children lost their protective maternal antibody by the age of 4 months only 3% had enough antibodies to protect them between the ages of 6-9 months.

Nevertheless, in West Africa, measles vaccine is given at 9 months of age which based on an early serological study in Kenya is thought to be the optimal age for protection against measles in endemic areas where maternally derived antibody

as a result of natural measles may inhibit the vaccine[8].

Since then as coverage has increased and the majority of mothers are now vaccinated which has resulted in lower concentrations of measles antibody transferred to their infants and a lower age of susceptibility to measles[9]. Surprisingly, there have been few papers from sub -Saharan Africa which have documented this phenomenon even though it is known that during outbreaks of measles the incidence of measles and mortality is high in young infants. An implication of these observations was that lowering the age of measles vaccination might be beneficial[9].

In Nigeria, infants are vaccinated against measles at the age of 9 months. However, persistence of maternal antibodies has been correlated with vaccination failure among infants less than a year of age, thereby making a mockery of vaccination of infants under the age of one year[10, 11]. Vaccine- induced immunity also appears to be shorter lived than one engendered by wild virus, suggesting that infants of vaccinated mothers may lose passively acquired antibodies faster than those of previously infected mothers[6].

A considerable number of cases of measles occur during the first year of life although overt measles before the age of 6 months is rare because of the supposed protection provided by the maternal antibodies[12]. Measles takes a serious course and may lead to death in children between 1-5 years and factors not yet identified converge to give this effect[12, 13].

Infection with wild measles virus causes extensive mobilization of the immune defenses[12]. Subclinical infections in non-immunity such as maternal antibodies or active immunity may have virus replication in the body cause mild or no clinical symptoms[12]. After a regular infection, Black and Rosen[14] showed that titers of antibodies be demonstrated throughout life in essentially all cases even in the absence of re-exposure[12].

According to Odomele et al.[12], development of immunity to this disease is either congenital, vaccination or infection by wild type. The sources of maternally transmitted antibodies in children are the antibody transferred in utero via the placenta and the colostrum (breast milk)[12]. The probability of this transmission is a function of complexity and class of the antibodies[12].

Several studies showed in utero transmission as the only source by which mothers transmit antibodies to their children[12] while Adu and Adeniji[15] showed children derive maternal antibodies from breast milk when sucking. Placental transfer of immunoglobulin antibodies is a function of complexity and class of the antibody. The role of maternal antibodies in the seroconversion to measles vaccination is documented[12, 15].

Thus, this paper touches on an important and under researched topic. This study aimed at determining the level of low pre-vaccination measles antibody among infants receiving measles immunization in Ilorin, Kwara State, Nigeria. It also evaluated the prevalence of low pre-vaccination measles antibodies in the sera of children

brought for measles vaccination and established the rate of seroconversion to measles vaccination in children of nursing mothers. It also evaluated the potency of the vaccine in relation to seroconversion.

2. Materials and Methods

2.1. Study Population

Ethical consideration was sought and obtained from the UITH Ethical Research Committee. Pre-vaccination blood samples were obtained from 400 infants brought to the EPI Clinic of the University of Ilorin Teaching Hospital, Ilorin, Kwara State, Nigeria.

2.2. Sample Collection

Blood samples were collected by finger puncture onto ROPACO (Rochester, USA) rectangular filter paper measuring 7 cm by 10 cm as described by Nakano et al.[16]. Other information like name, age, sex, date of vaccination was also recorded on the filter paper. The filter papers were dried at ambient temperature and stored in plastic bags at -20℃ until ready for serum extraction.

2.3. Collection of Epidemiological Data

Age, sex, breast feeding pattern and previous history of measles were collected using a Performa specially designed for this study.

2.4. Source of Antigen

The antigen used, was obtained from the measles vaccine collected from the National Program on Immunization unit (NPI) of University of Ilorin Teaching Hospital, Ilorin, Kwara State, Nigeria. The Measles vaccine which is live attenuated (Freeze-dried) is prepared from the Edmonston strain of measles virus attenuated by twenty-two passages on human diploid cells (HDC) and is known as the Edmonston – Zagreb strain. The lyophilized vaccine is provided with diluents and the vaccine meets the requirement of WHO when tested by the method outlined in WHO requirement for vaccine production[17, 18].

2.5. Potency of the Vaccine

Each single human dose of the vaccine contains 1000CCID50 of live virus particles when reconstituted in a volume of 0.5ml. Stability data shows that the vaccine retains the potency of 1000CCID50 per dose after 1 week at 37ºC[17-20].

2.6. Cultivation of the Antigen

Measles antigen was prepared by inoculation of Edmonston strain of measles vaccine on Vero/SLAM cells (10^6cells/ml). The serum titer was expressed as the highest dilution of the serum showing complete inhibition of hemagglutination. A grown monolayer of Vero/SLAM cell in a tissue culture bottle obtained from the tissue culture unit

of World Health Organization National Polio Laboratory, Department of Virology, University of Ibadan, Ibadan, Nigeria was used for the inoculation of the vaccine antigen. After 72hrs, maximum development of the CPE was observed using an inverted microscope. The tissue culture growth was then frozen and thawed three times to reduce the virulence of the virus. The measles virus culture was then centrifuged at 3000rpm for 20 minutes using a refrigerating centrifuge to obtain suspension of the viral particles which were then dispensed in aliquots of 1mls into cryovials, and stored in the freezer, ready for use[17-20].

2.7. Susceptible Erythrocyte

The susceptible erythrocyte (Red blood cell) was used as described by Hsiung and Fong[21].

2.8. Vaccine Titration

The vaccines were titrated as previously described by Onoja et al.[22]. The vaccine titer was calculated by the method of Reed and Muench[23].

2.9. Serological Analysis

Haemagglutination inhibition test (HI) was used to measure the measles antibodies as described by Brooks *et al.*[24] and the resulting titers from the various assays are as contained in the table of results. About 0.025ml of 0.05ml of 1:10 dilution of sera was mixed each with 0.025ml of PBS/BSA (pH 7.2) of the 4HA (haemagglutinating) units of commercially available measles antigen. This gave a range of serial two-fold dilution of 1:10 to 1:256, except the controls. The plates were shaken and mixture incubated at 37^OC for one hour. About 0.05ml of 1% washed AGM-RBC was added and kept at 37℃ until the cells in the control wells had settled at the bottom before results were read. The serum HI titer was expressed as the highest dilution of the serum showing complete inhibition of haemagglutination. Measles virus antibody ≥40 HI titer is the study threshold of protection against measles. Measles virus antibody of <1:10 HI titer was considered to be undetectable while 1:10 to 1:20 HI titer was considered to be low titer.

2.10. Data Analysis

Identification of factors that may correlate with the seroconversion was carried out by the Chi-square (X^2) distribution method using Microsoft Excel. Confidence interval was set at p≤ 0.05. In the analysis, I used <1:10 as negative and ≥ 1:10 as positive in order to get valid inferential analysis.

3. Results

The three vials of vaccine strain of measles virus cultured in Vero/SLAM cells had virus titer values of 3.5, 3.25 and 3.5 Log which is according to the WHO minimum standard

of 3.0Log (1000CCID$_{50}$) per human dose.

3.1. Prevaccination Measles Antibody Titer

Of all the 400 infants screened for pre-vaccination antibodies, 371/400(92.8%) had measles virus antibody titer which ranged from <1:10 to 1:20 while the remaining 29/400 (7.2%) had measles virus antibody titer of ≥1:40. It showed that 215(53.7%) children of all ages had no detectable prevaccination antibodies titer.

3.2. Sex Distribution of Infants

A total of 400 infants were recruited into the study over the period of 12 months. Among the pre-vaccination group, there were 245/400(61.3%) males and 155/400(38.7) females, giving a male to female ratio of 1.6: 1.

3.3. Age Distribution of Infants

The age distribution of the infants recruited into the study were as follow; the majority, 236/400 (59.0%) were aged 9 months, 84/400 (21.0%) were aged 10 months. The others were 56/400 (14.0%) eleven month olds and 24/400 (6.0%) twelve month old infants (Table 1).

3.4. Measles Virus Antibody Titer According to Age

Among the 9 month old infants, only 15/236(6.4%) still had high measles antibodies of 1:40 pre-vaccination, 91/236 (38.6%) had low maternal antibodies which ranged from 1:10 to 1: 20 while the remaining 130/236 (55.1%) had no detectable measles virus antibody titer as shown in Table 1. Children within 10 years of age had higher prevalence of prevaccination antibody titer (≥1.40) while children 12 years of age had higher prevalence of no detectable prevaccination antibody titer. However, there is no significant difference in the level of pre-vaccination antibody titer among the various age groups (X^2 = 7.267, P-value = 0.839).

Table 1.   Pre-Vaccination Measles Virus Antibody Titer According to the Age of Infants

Age (months)	No. tested (%)	Pre-vaccination Measles Virus Antibody titer (%)			
		<1:10	1:10	1:20	≥1:40
9	236(59.0)	130(55.1)	59(25.0)	32(13.6)	15(6.3)
10	84(21.0)	44(52.4)	19(22.6)	12(14.3)	9(10.7)
11	56(14.0)	27(48.2)	14(25.0)	11(19.6)	4(7.1)
12	24(6.0)	14(58.3)	3(12.5)	6(25.0)	1(4.2)
Total	**400(100.0)**	**215(53.7)**	**95(23.7)**	**61(15.3)**	**29(7.3)**

X^2 = 7.267, P-value = 0.839

3.5. Measles Virus Antibody Titer According to Sex

Among the male infants, 133/245(54.3%) had pre-vaccination measles virus antibody titer of < 1:10, 60/245 (24.5%) had antibody titer of 1:10, 37/245 (15.1%) had titer of 1:20, while the remaining 15/245(6.1%) had antibody titers of ≥1:40. In the same vein, 82/155 (52.9%) females had no detectable antibody titer, 35/155(22.6%) had antibody titer of 1:10, 24/155 (15.5%) had titer of 1:20, while 14/155 (9.0%) had titer of ≥1:40 (Table 2).

3.6. Impact of Previous Measles Infection on Pre-vaccination Antibody Titer

Only 31/400(7.8%) of the vaccinees had previous history of measles prior to vaccination while the remaining 369/400 (92.2%) had no history of measles. Twenty two (70.9%) of the 31 vaccinees with previous history of measles had pre-vaccination measles virus antibody titer of $\geq$1:40. Of the 369 infants without a previous history of measles, only 7(1.9%) had protective pre-vaccination antibody titer (Table 3). There was significant difference in the level of pre-vaccination measles virus antibody among the group that had previous history of measles (X^2 = 34.507, P-value = 0.0005).

3.7. Impact of Exclusive Breastfeeding on Pre-vaccination Antibody Titer

All the 400 infants were breastfed. A total of 189 (47.3%) infants were breast fed exclusively while 211(52.8%) were non-exclusively breast fed (Table 4). Twelve (6.3%) of the 189 that were exclusively breast fed had protective pre-vaccination antibody titer, while 17 (8.1%) of the 211 non-exclusively breast fed infants had protective antibody titer (Table 4). There was no significant difference in the level of pre-vaccination antibody titer among the infants that were exclusively breast fed and those that were not (X^2 = 6.617, P-value = 0.470)

4. Discussion

The study showed that of all the 400 infants screened for pre-vaccination antibodies, 92.8% had low pre-vaccination measles antibody titer which ranged from <1:10 to 1:20 while the remaining 7.2% had protective antibody titer of $\geq$1:40. It also showed that the lowest pre-vaccination antibodies titer was 4 and the highest titer was 256. This HI antibodies clusters agrees closely with the report of Deepti et al.[25], Akyala et al.[19], Motayo et al.[26] and Ogundiji et al.[27]. This agreement may be due to the same haemagglutination inhibition serological technique employed[19, 26, 27]. The Haemagglutination inhibition (HI) test is the most widely acceptable test in most developing countries like Nigeria[26]. HI test has long for a long time a gold standard for laboratory diagnosis of measles infection [26]. This is because it is very sensitive and specific and easily performed in any laboratory[26].

Table 2. Pre-Vaccination Measles Virus Antibody Titers According to the Sex of Infants

Sex	No. Tested (%)	Pre-Vaccination Measles Virus Antibody (%)			
		<1:10	1:10	1:20	$\geq$1:40
Males	245(61.3)	133(54.3)	60(24.5)	37(15.1)	15(6.1)
Females	155(38.7)	82(52.9)	35(22.6)	24(15.5)	14(9.0)
Total	**400(100.0)**	**215(53.7)**	**95(23.7)**	**61(15.3)**	**29(7.3)**

X^2 =9.287, P-value = 0.199

Table 3. Impact of Previous Measles on Pre-Vaccination Measles Virus Antibody Titer

History Of Measles	Total (%)	Pre-Vaccination Measles Virus Antibody Titer (%)			
		<1:10	1:10	1:20	$\geq$1:40 (%)
No	369(92.3)	214(99.5)	92(96.8)	56(91.8)	7(13.8)
Yes	31(7.7)	1(0.5)	3(3.2)	5(8.2)	22(75.9)
Total	**400(100.0)**	**215(53.7)**	**95(23.7)**	**61(15.3)**	**29(7.3)**

There was an association (P=0.0005; X2 = 34.507) between previous history of measles and proportion of measles virus HI antibody.

Table 4. Impact of Exclusive Breastfeeding on Pre-Vaccination Antibody Titer

Age (months)	Total (%)	No. Exclusive breastfeeding	No. Mixed feeding	PRE-VACCINATION MEASLES VIRUS ANTIBODY LEVELS (%)							
				<1:10		1:10		1:20		$\geq$1:40	
				E	M	E	M	E	M	E	M
9	236(59.0)	122(51.7)	114(48.3)	71(30.1)	59(25.0)	34(14.4)	25(10.6)	14(5.9)	18(7.6)	3(1.3)	12(5.1)
10	84(21.0)	42(50.0)	42(50.0)	20(23.8)	24(28.6)	7(8.3)	12(14.3)	9(10.7)	3(3.6)	6(7.1)	3(3.6)
11	56(14.0)	20(35.7)	36(64.3)	10(17.9)	17(30.4)	6(10.7)	8(14.3)	2(3.6)	9(16.1)	2(3.6)	2(3.6)
12	24(6.0)	5(20.8)	19(79.2)	1(4.2)	13(54.2)	2(8.3)	1(4.2)	1(4.2)	5(20.8)	1(4.2)	0(0.0)
Total	**400(100.0)**	**189(47.3)**	**211(52.7)**	**102(25.5)**	**113(28.3)**	**49(12.3)**	**46(11.5)**	**26(6.5)**	**35(8.8)**	**12(3.0)**	**17(4.3)**

X^2 = 1.327, P-value = 0.723
KEY: E – Exclusive breastfeeding, M – Mixed feeding; Protective pre-vaccination antibody titer ($\geq$1:40), Low protective pre-vaccination antibody titer (<1:40)

The non-protective level of measles antibody among majority (92.8%) of these infants puts them at risk of developing measles even before they are due for their measles vaccination. This is further justified by the fact that 31(8.0%) of these children were said to have had measles prior to the time they were brought for vaccination at nine months, it was however difficult to rule out measles like illnesses as none of the cases were confirmed using serology or culture. Kamel *et al.*[28] and Hegazy *et al.*[29] had also previously reported pre vaccination measles antibody titer of 8.3% and 8.2% respectively in two separate studies carried out in Saudi Arabia. It is however interesting to note that those infants with previous history of measles showed a statistically significant pre vaccination measles antibody level when compared with those without previous history of measles. Studies have shown that children with naturally acquired immunity often have significantly higher antibody titer than children with vaccine induced immunity[30].

This study also showed that 53.7% of the children of all age groups had no detectable prevaccination antibody titer. The outcome of the undetectable antibodies and some low titer across the groups especially when it is noted that all these children have received measles vaccination at 9 months of age indicates a possibility of some primary vaccine failure[19], which could be due to persistence of maternal antibodies[19, 31] or improper storage and handling of vaccine[11, 19] receipt of immunoglobulin[19], genetic factors and other incompletely understood factors[19, 32] or cases of non-vaccination or religious or political objections [19, 33]. This therefore emphasizes the need for surveillance and improvement of the vaccination program[19].

The age-dependent prevalence showed that among the 9 month old infants, only 6.4% still had high pre-vaccination measles antibodies titer of 1:40 while remaining 55.1% had no detectable pre-vaccination measles antibodies titer. It also showed that children within 10 years of age had higher prevalence of prevaccination antibody titer ($\geq$1.40) while children 12 years of age had higher prevalence of no detectable prevaccination antibody titer. However, this differences is not statistically significant (P-value = 0.839). This is inconsonance with previous study by Itoh et al.[34] who identified a decline in the antibody titer as the children grew, until subjects reached the age of 15 to 19 years of age, and then increase again during their twenties. Our present findings deviate from that of Akyala et al.[19] who observed that distribution of measles HI antibodies increase simultaneously among the age groups, with the highest percentage antibodies titer among age group 12-16years. It is also important to observe that not all children who received a single dose vaccine at nine (9) months of age will develop a protective response[19].

In this study, 55.1% of 9 months old infants had no detectable antibody titer or had a titer less than 1 in 10 which presumably means that the test at this starting dilution was negative. This is in consonance with previous studies in other areas of West Africa which shows that at 9 months of age in over 80.0% of infant's measles antibody is undetectable[35].

A recent study from Guinea Bissau showed that over half of infants had no detectable HAI antibody at 4.5 months of age and concluded that early measles vaccination not only saved deaths from measles in infancy but had non-specific beneficial effects on childhood survival[9].

The sex-dependent prevalence showed that among the male infants, 54.3% had pre-vaccination measles antibody titer of < 1:10 while the remaining 6.1% had pre-vaccination measles antibody titer of $\geq$1:40. In this study, the total number of children with undetectable antibody was 215, of this 82(38.1%) were females. The proportion of 155 female children with no detectable antibody is 82/155 (52.9%). Generally from the distribution of measles HI antibodies titer according to sex, it was observed that females had more antibodies than the males among the subjects assayed. Statistically, this was not significant at P value = 0.199. In consonance with a previous study by Ogundiji et al.[27], sex (p=0.199) was not significantly associated with the level of measles antibody. This is a deviation from what was reported by Akyala et al.[19] who observed that males had more antibodies than the females among the subjects assayed. A report by Chen[36] identified excess mortality following acute measles infection among females at all ages.

In this study, 7.8% of the vaccinees had previous history of measles prior to vaccination while the remaining 92.2% had no history of measles. The study also showed that 70.9% of the 31 vaccinees with previous history of measles had pre-vaccination measles virus antibody titer of $\geq$1:40. Of the 369 infants without a previous history of measles, only 7(1.9%) had protective pre-vaccination antibody titer. There was significant difference in the level of pre-vaccination measles virus antibody among the group that had previous history of measles (P-value = 0.0005). The presence of HI measles antibody in these children without previous history of measles vaccination was an indication of circulation of wild measles virus in the environment[12, 19]. Also, since specific antibodies presence in breast milk of mothers depends on previous contact with the microorganism or vaccination antigen[12, 19], our result confirmed widespread measles virus in the local population.

The pre-vaccination measles antibody detected in some of the study children may have been maternally derived as majority of the mothers (7.8%) had measles vaccination while they were young. Hence, offsprings of such women lose their transplacental antibodies earlier than the offsprings of unvaccinated mothers[37]. In contrast, Adu *et al.*[8] have shown that measles antibodies found in children earlier than 9 months may not always be maternally derived. It is also possible that the antibodies were acquired post exposure to circulating wild measles as it is known that measles is endemic in Nigeria. Contrary opinions from Onoja et al.[22] and Albrecht et al.[38] have revealed maternal antibody presence at 12 months.

This study showed that all the 400 infants were breastfed, of which 47.3% were breast fed exclusively while 52.8% were non-exclusively breast fed. It showed that 6.3% of the 189 that were exclusively breast fed had protective

pre-vaccination antibody titer while 8.1% of the 211 non-exclusively breast fed infants had protective antibody titer. However, this difference was not statistically significant (P-value = 0.470). Adu and Adeniji[15] reported lack of complement fixation (CF) antibodies in children of corresponding positive mothers, suggesting very little or no antibody was passed to children through breast milk. Ogra et al.[39] observed very low transfer of antibodies in humans through breast milk. However, Onoja et al.[22] observed higher antibody level in children who had longer breastfed. Our study showed nonsignificant difference between controls and patients who were breast fed.

There was no significant difference in pre vaccination antibody titer among the infants that were exclusively breastfed and those that were not. This finding is contrary to the belief that infants that are exclusively breastfed have better passive immunity compared with those that had mixed feeding[22, 40]. According to Aaby et al.[9], although the overall effect did not reach statistical significance, the results may indicate that a two dose schedule with Edmonston-Zagreb measles vaccine given at 4.5 and 9 months of age has beneficial nonspecific effects on children's survival, particularly for girls and for children who have not received neonatal vitamin A.

In Mozambique, vaccine coverage has been insufficient to interrupt measles transmission[41]. Enhanced surveillance, including investigation of cases and outbreaks, and improvements in measles vaccination[41]. Cost - effectiveness of the SIA child health delivery platform varies substantially across SA provinces, and it is substantially more cost-effective when vitamin A supplementation is included in the interventions administered[41]. Cost - effectiveness assessments should consider health system delivery platforms that integrate multiple interventions, and they should be conducted at the sub-national level[42].

Ntshoe et al.[43] observed a reduction in measles incidence following the nationwide mass vaccination campaign even though it was conducted approximately one year after the outbreak started. According to their findings, a booster dose at school entry may be of value given the high incidence in persons >5 years[43].

The study therefore raises the need for a second dose of vaccination according to WHO recommendation[32]. Before the age of two years or at a later years or a more appropriate period to reduce the number of primary vaccine failure and or cases of non-vaccination and to boost titers in all children and age groups[32]. This is the practice in several developed countries including United States which have helped to achieve a substantial reduction in the incidence of measles due to the initiation of a two dose measles vaccine strategy[34].

The finding in this study that majority of the infants had low non protective antibody titer by the time they were due for the 9 months measles vaccination suggests that infants less than 9 months are poorly protected against measles. Furthermore, the alternative strategy which is advocated by WHO is to increase coverage at 9 months and conduct catch up vaccination campaigns thus maintaining herd immunity and protecting the young. However, in order to achieve the WHO goal of eradicating measles globally, there is therefore need to consider the development of a safe and immunogenic measles vaccine which can be administered to young infants less than 9 months old.

In conclusion, this study showed that 92.8% had low pre-vaccination measles antibody titer (<1:10 to 1:20). It also showed that 7.2% had protective antibody titer of 1:40. The non-protective level of measles antibody among majority (92.8%) of these infants puts them at risk of developing measles even before they are due for their measles vaccination. This observation strengthens the need to accelerate global measles control activities. More aggressive childhood vaccination programs, introduction of a two dose schedule and successful mass vaccination campaigns be conducted in Ilorin, Kwara State, Nigeria.

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REFERENCES

[1]   Maldonado, Y. Measles in: Berhaman, R.E., Kleigman, R.M., Jensen, H.B. Nelson extbooks of Paediatrics .17th Ed. Philadelphia; Saunders (Publishers) 2004;1026-1031.

[2]   Commey, J.O., Dekyem P. Measles in Southern Ghana; 1985-1993, W. Afr J Med.1994; 13:223-226.

[3]   Centre for Disease Control (CDC) Update: Global measles control and mortality reduction worldwide, 1991-2001. Morbidity, Mortality, Weekly Rep. 2003; 52: 471-475.

[4]   Oyedeji, O. A., Elemile, P.O., Fadero, F.F., Oninla, S.O., Joel-Medawese, V.I., Oyedeji, G.A. Measles among hospitalized children in Nigeria. Int. J. Paed and Nephrol. ISSN 1528-8321. 2007; 7 (1).

[5]   Centers for Disease Control and Prevention. Recommended immunization schedules for persons aged 0 through 18 years. United States, 2009. CDC Recommended Vaccine Schedule. Dec 2008; 57(51-52)

[6]   Oyedele, O.O., Odemuyiwa, S.O., Ammerlaan, W, Muller, C.P., Adu, F.D. Passive immunity to measles in the breast milk and cord blood of some Nigerian subjects. J. Trop Paediatr. 2005;51: 45-48.

[7]   Okonko, I.O., Nkang, A.O., Udeze, A.O., Adedeji, A.O, Ejembi, J, Onoja, B.A et al. Global eradication of measles: A

highly contagious and vaccine preventable disease- What went wrong in Africa? *J Cell and Animal Biol*. 2009a; 3 (8); 119-140.

[8]   Adu, F.D., Odoemele, F.C., Bamgboye, E. Effect of measles antibodies in the breast milk and sera of mother on seroconversion to measles vaccine. *Afr J Biomed Res*. 1999; 2(1) : 7-11.

[9]   Aaby P, Martins CL, Garly ML, Balé C, Andersen A, Rodrigues A, Ravn H, Lisse IM, Benn CS, Whittle HC. Non-specific effects of standard measles vaccine at 4.5 and 9 months of age on childhood mortality: Randomised controlled trial. BMJ, 2010; 341: c6495.

[10] Baba MM, Omede SC, Omotara BA, Ambe JP. 2007. Evaluation Of Measles Vaccines In Northeastern Nigeria. Nature and Science;5(3):49-53.

[11] Meissner HC, Strebel PM, Orenstein WA. 2004. Measles vaccine and the potential for a worldwide eradication of measles. Nature and Science, 114(4):1065-1069.

[12] Odoemele CF, Ukwandu NCD, Adu FD, Nmorsi OPG and Omotade OO. 2006. Effect of Measles Virus Antibodies from Breast Milk of Nursing Mothers on Seroconversion of Children After Measles Vaccination. Shiraz E-Medical Journal, 7(2): 1-10

[13] Morley, P (1975): Overview of the present situation as to measles in the developing World. Trans. R. Soc. Trop. Med. Hyg., 69:22-23.

[14] Black, FL and Rosen, L (1962): Patterns of measles antibodies in residents of Tahiti and their stability in the absence of re-exposure. J. Immunol., 88:725-731.

[15] Adu, FD and Adeniji, JA (1995): Measles antibodies in the breast milk of nursing mothers. Afr. J. Med. Med. Sci., 24:385-388.

[16] Nakano, J.H., Miller, D.L., Foster, S.O. and Brink, E.W. Micro-titer determination of Measles Hemagglutination Inhibition with filter paper. *J Clin Microbiol*. 1983; 17(5): 860-863.

[17] World Health Organization (WHO). 1997. Manual of laboratory methods for potency testing of vaccines used in the World Health Organization Expanded Program on Immuunization, 1997. WHO/VSQ/97.04.

[18] World Health Organization (WHO). 1994 Measles, Mumps and Rubella vaccine use and strategy. Requirements for vaccine production TRS 840.

[19] Akyala IA, Obande G, David Ishaleku. 2013. Measles Heamaglutination Inhibition (HI) Antibodies Titers among Persons Age 2-21years In Lafia, Nasarawa State, North Central Of Nigeria. International Journal of Advanced Research, 1(5): 8-12.

[20] World Health Organization (WHO). Manual for the Virological Investigation of Measles. Geneva, Switzerland: World Health Organization, 2004.

[21] Hsiung GD, Fong CKY (1982) Haemagglutination inhibition by measles virus. In: Diagnostic virology by Yale University 3rd ed. Pp. 151-161. Murray Printing Co. Westford United State.

[22] Onoja, AL; Adu, FD and Tomori, O (1992): Evaluation of measles vaccination programme conducted in two separate centres. Vaccine, 10(1): 49-52.

[23] Reed LJ and Muench H (1938). A Simple Method Of Estimating Fifty Percent End Points. AM. J. HYG. 27, 493-497

[24] Brooks GF, Butel JS, Morse SA (2004) Measles. In: Medical Microbiology 23rd ed. Pp. 562-565. Appleton and Lange.

[25] Deepti Rawat, Anita Chakravarti, Sangita Tadav (2001) Measles antibodies. *Indian Pediatrics*; 38: 1286-1289.

[26] [26] Motayo BO, Okonko IO, Faneye A and Adu FD. Preparation Of High Potent Measles Haemagglutinating Antigen From Wild Type Measles Virus In Ibadan, Nigeria. *New York Science Journal 2011;4(12):30-37.*

[27] Ogundiji OT, Okonko IO, and Adu FD. Determination Of Measles Haemagglutination Inhibiting Antibody Levels Among School Children In Ibadan, Nigeria. *Journal of Immunoassay and Immunochemistry, 2013; 34:208-217.*

[28] Kamel, ML. Comparison of some epidemiological characteristics of vaccinated and unvaccinated cases in Saudi Arabia. *Alex J Paed*. 1999; 3(4): 542-545.

[29] Hegazy, I.S. A Sero-epidemiological study of measles: practical implications for measles immunization. *Saudi Arabia Health Science J East Med Reg. 1999; 7(2) : 62-70.*

[30] Okonko IO, Onoja BA, Adedeji AO, Ogun AA, Udeze AO, Ejembi J, Garba KN, Egun OC, Fowotade A. 2009b. The Role of Vaccines in Elimination and Global Eradication of Measles- A Review of Literature. *African Journal of Pharmacy and Pharmacology, 3(9):* 413-425

[31] Wood LD, Brunnel PA (1995) Control in the united State: Problems of Nature and Science, the Past and challenges for the future. In Clinical microbiology Review, 260-267.

[32] IRIN (2005). Measles kills more than 500 children. Available at http://www.irinnews.org/report.aspx?reportId=535066.*en. wikipedia.org/wiki/Measles.*

[33] Helfand RF, Witte D, Fowlkes A, et al (2008). Evaluation of the immune response to a 2-dose measles vaccination schedule administered at 6 and 9 months of age to HIV-infected children in Malawi. *Journal of infectious diseases*; 198:1457-1465.

[34] Itoh M, Okuno Y, Hotta H (2002). Comparative analysis of titers of antibodies against Measles virus in sera of vaccinated and naturally infected Japanese individuals of different age groups. *Journal of Clinical Microbiology*; 40(5): 1733-1738.

[35] Njie-Jobe J; Nyamweya S; Miles DJ; van der Sande M; Zaman S; Touray E; Hossin S; Adetifa J; Palmero M; Burl S; Jeffries D; Rowland-Jones S; Flanagan K; Jaye A; Whittle H. Immunological impact of an additional early measles vaccine in Gambian children: responses to a boost at 3 years. Vaccine, 2012; 30:2543-2550.

[36] Chen SSP, Fennelly GJ (2009) Measles: an overview. Updated June 10th, 2009. Available at www.health.vic.gov.a u/idea/bluebook/measles.

[37] Aref , E. Detecton of the presence of measles antibodies in vaccinated children*. Alex J Paed*. 1989; 3: 165-169.

[38] Albrecht P, Ennis FA, Saltzman EJ, Krugman S (1977).

Persistence of maternal antibodies. Mechanism of measles vaccine failure. *Journal of Pediatric*; 91:715-718.

[39] Ogra, SS; Weintraub, D and Ogra, PL (1977): Immunologic aspects of human colostrum and milk. J. Immunol., 119:245-248.

[40] Mulders MN, Nebie YK, Fack F, Kapitanyuk T, Sanou O, Valea DC, *et al.* Limited diversity of measles field isolates after a national immunization day in Burkina Faso: progress from endemic to epidemic transmission? *J Infect Dis* 2003; 187 suppl 1:S277-82.

[41] Muloliwa AM, Camacho LA, Verani JF, Simões TC, Dgedge Mdo C. Impact of vaccination on the incidence of measles in Mozambique in the period 2000 to 2011. Cad Saude Publica.

2013 Feb;29(2):257-69.)

[42] Verguet S, Jassat W, Bertram MY, Tollman SM, Murray CJ, Jamison DT, Hofman KJ. Supplementary immunization activities (SIAs) in South Africa: comprehensive economic evaluation of an integrated child health delivery platform. Glob Health Action. 2013 Mar 1;6:1-9. doi: 10.3402/ gha. v6i0. 20056

[43] Ntshoe GM, McAnerney JM, Archer BN, Smit SB, Harris BN, Tempia S, Mashele M, Singh B, Thomas J, Cengimbo A, Blumberg LH, Puren A, Moyes J, van den Heever J, Schoub BD, Cohen C.Measles outbreak in South Africa: epidemiology of laboratory-confirmed measles cases and assessment of intervention, 2009-2011. PLoS One. 2013;8(2): e55682.