Evaluation Of Measles Vaccines In Northeastern Nigeria

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ABSTRACT: Measles account for nearly half of the 1.7 million annual deaths due to childhood vaccine-preventable diseases. This study was designed to assess the sero-conversion rate of a single dose measles vaccine on children aged 9-12 months. The pre and post measles vaccination sera of the children as well as sera of some of the vaccinees' mothers were tested using the heamagglutination inhibition test. Of the 136 prevaccination sera, 26 (16.9%) had measles HI antibody with Geometric mean titer (GMT) of 36.4 while only 22 (23%) of 100 post vaccination sera had antibody against measles virus and having a GMT of 22.9. The measles HI antibody between the mothers' and pre vaccination sera of the children was not significantly different (Kw> 3.000 df. 2, P= 0.022313). However, five mothers and their corresponding children had measles antibody with the GMT of 21.1 and 9.2 respectively. Also, five seropositive mothers (GMT= 55.7) had seronegative children. Nevertheless, 11 of 60 (18.3%) seronegative mothers had seropositive children with GMT 14.1. Ten children (14.3%) had clinical measles infections before they were brought for vaccination at the age of 9 months. In addition 13 (18.6%) had index cases of measles in their families. No significant difference was observed between measles antibody (pre-vaccination) and previous clinical measles infection (t= 0.23730, df. 24, P= 0814519). Although varied titers of measles vaccines, (ranging from $10^{1.5}$ to $10^{6.0)}$ were observed in all the centers chosen for the study. There was however no significant difference in titres among the various vaccination centres ($P > 0.05$). There is need to give quality measles vaccine whether single or supplementary dose if the global effort to reduce measles by 95% in Africa is to be achieved. [Nature and Science. 2007;5(3):49-53]. (ISSN: 1545-0740).

Keyword: Measles, vaccines, children, Nigeria

1. INTRODUCTION

It was observed that countries with a single-dose on measlesare not only the poorest and least developed, but report the lowest routine vaccination coverage and experience the highest measles diseases burden. (International Note 2002). Yet not all children who receive a single measles vaccine at 9 months of age will develop a protective response and are the primary vaccine failure (WHO 2001). These authors attributed primary vaccine failure to the presence of maternal antibody at the time of vaccination, damaged vaccines; receipt of immune globulin, genetic factors and other incompletely understood factors (Meissner et al 2004). Therefore a small proportion of individual who remain susceptible due to primary vaccine failure will accumulate over time. When exposure occurs, the contagiousness of measles virus may result in an outbreak even when only a small number of case contacts are susceptible. It was then concluded that prevention of endemic measles transmission is not possible in countries with a single-dose immunization program, even when vaccination rates approach 100% (Meissner et al 2004). This study was designed to assess the sero-conversion rate of a single dose measles vaccine on children aged 9-12 months.

2. MATERIALS AND METHODS

STUDY POPULATION:

Children aged 9 months and above attending immunization centers such as Specialist Hospital (SH), University of Maiduguri Teaching Hospital (UMTH), Yerwa Clinic (YC), and Bolori Clinic (BC), Maiduguri were recruited for the study. The SH and YC represent all-purpose hospital center with the

vaccinees mainly from the lower and middle socio-economic classes of the population. However, UMTH represent an institution-based health center with the vaccinees cutting across the middle and upper socio-economic classes. BC represents polyclinic with vaccinees also cutting across the middle and the upper classes of the population.

VACCINES:

Measles vaccines for a day's vaccination exercise from three tier of immunization centers namely Epidemiological Unit (Epid unit) with the storage facility of all vaccines allocated for Borno state, University of Maiduguri Teaching Hospital (UMTH) representing the Tertiary, Specialist Hospital (SP) representing the Secondary and Yerwa Clinic representing primary Immunization centers. In the course of collection of the vaccines, cold chain maintenance was also monitored at different period of the day .The management; storage and handling of the vaccines in each center were monitored by observation, questioning and counseling where necessary. Also aliquots of reconstituted and vials of unreconstituted measles vaccines were collected in few cases. The vaccines were transported in a vaccine carrier box to the WHO National Polio laboratory where they were stored at -20^0C until tested.

SERA:

One hundred and thirty-six children (aged 9-12 months) were bled for measles pre-vaccination sera. Of these 136 children, sera were also taken from 70 of the vaccinees'mothers. Four weeks later, 100 of the same children were bled for post vaccination sera. Serum samples were collected by finger prick method in Rapocca filter paper,) Rochester,Ml,USA) , dried at ambient temperature and stored in plastic bags at – 20^0C . Sera were extracted from the filter paper as previously described by Nakano et al (1983). All sera were heat inactivated at 56^0C for 30 minutes, treated with 25% kaolin to remove non-specific inhibitor and was absorbed with 50% monkey red blood cells (RBC) to remove non-specific agglutinins.

HAEMAGGLUTINATION TEST (HA) and HAEMAGGLUTINATION INHIBITION (HI) TEST:

The measles antigens used in the test were supplied by Dr Yoshi, JICA in Collaboration with World Health Organization (WHO) during a training course at Nogushi Memorial Medical Research Institute, Ghana 2001. The HA and HI test were carried out using WHO standard method and as described by Munube, 1979

VACCINE TITRATION:

The vaccines were titrated as previously described by Onoja et al 1992. The vaccine titer was calculated by the method of Reed and Muench (1938).

VACCINEES' PERSONAL DATA:Such data was based on questionnaire survey. The information collected from the Vaccinees include name, date of birth, sex, vaccination history, history of measles before the study if any and the age it occurred. Identification of the source of measles infection was also obtained (i.e. as an index case which is the first case in a household, or as a secondary case which is a child who develops measles between 6 to 20 days after the index case and under the same roof.)

3. RESULTS

Table 1 shows the HI antibody in children pre and post measles vaccination. Out of 236 children tested, 26 (16.9%) and 22 (23%) had measles HI antibody with GMT of 36.4 and 22.9 pre and post measles vaccination respectively. In table 2, measles HI antibody profile in mother-child pair is presented. Of 70 mothers tested, only 10 had HI measles antibody with GMT 34.3. Five mothers and their corresponding children had measles antibody with the GMT of 21.1 (mothers) and 9.2 (children pre vaccination) respectively. Also, five seropositive mothers (GMT= 55.7) had seronegative children. Nevertheless, 11 of 60 (18.3%) seronegative mothers had seropositive children with GMT 14.1 The HI antibody between mother and child (pre-vaccination) was not significantly different (Kw> 3.000 df. 2, P= 0.022313). In table 4 the potency of measles vaccines collected at different Immunization centers in Maiduguri Metropolitan is presented. Although varied titers of measles vaccines, (ranging from $10^{1.5}$ to $10^{6.0)}$ were observed in all the centers chosen for the study but they were not significantly different ($P > 0.05$).

The responses of vaccinees' mothers on clinical measles among Vaccinees and other children in the family:- Ten children (14.3%) had clinical measles infections before they were brought for vaccination at the age of 9 months. In addition 13 (18.6%) had index cases of measles in their families. No significant

difference was observed between measles antibody (pre-vaccination) and previous clinical measles infection (t= 0.23730, df. 24, P= 0814519).

Sex distribution of measles HI antibody:

Out of 134 males tested, 28 (20.9%) and 20 (19.6%) of 102 females had measles HI antibody Pre and post vaccination and the sex of the vaccinees were not significantly different from the measles antibody. Age at which measles occurred in index cases: The age at which index cases occurred in the family was significantly different from the titer of HI measles antibody pre-vaccination (F= 623432.600, df 4, P=0.00002).

Table 1. Measles Hi Antibody In Children Pre And Post Vaccination

Vaccination status	NO. tested	No. positive	Titres								
			4	8	16	32	64	128	256	1024	mean titre
Pre – vaccination	136	24 (17.6)	-	4	9	1	4	2	-	4	371.3
Post – vaccination	100	24 (24)	1	1	9	6	1	5	-	-	44.0
Total	236	48 (20.3)	1	5	18	7	5	7	-	4	415.3

Table 2. Measles Hi Antibody Profile In Mother – Child Pair.

S/NO	ITEM	MOTHERS (GMT)	CHILD	
			PRE- VACCINATION (GMT)	POST VACCINATION (GMT)
1	No. tested	70	70	50
2	No positive	10 (34.3)	10 (36.8)	16 (11.8)
3	No positive mother/ positive children	5 (21.1)	5 (9.2)	5 (9.2)
4	No positive mother/ negative children	5 (55.7)	0 (0.0)	0 (0.0)
5	No positive children/ negative mother	0 (0.0)	5 (12.1)	11 (14.1)

Table 5: The Potency Of Measles Vaccines At Different Vaccination Centres In Maiduguri

S/No	DATE OF COLLECTION/ DATE OF TITRATION	SOURCE (VACCINATION CENTRES)	BATCH NO.	EXPIRATION DATE	MANUFACTURER	TITRE ($TCID_{50}$/DOSE)
1	21-09-01/26-09-01	EPU a	1690	JULY 2002	SERUM INSTITUTE OF INDIA	$10^{3.2}$
2	17-10-01/17-10-01	EPU	1686	,,	,,	$10^{2.0}$
3	5-12-01/5-12-01	EPU	1680	,,	,,	$10^{3.0}$
4	5-02-02/5-02-02	EPU	EU1866	,,	,,	$10^{2.8}$
5	12-10-01/ 12-10-01	UMTH b	EU1688	,,	,,	$10^{2.0}$
6	7-12-01/7-12-01	UMTH	1680	,,	,,	$10^{3.0}$
7	5-02-02/5-02-02	UMTH	1683	,,	,,	$10^{2.8}$
8	12-03-02/12-03-02	UMTH	1683	,,	,,	$10^{1.8}$
9	22-05-02/22-05-02	EPU	EU1866	May 2003	,,	$10^{3.0}$
10	26-06-02/26- 06-02	EPU	EU1863	May 2003	,,	$10^{2.8}$
11	5-02-02/5-02-02	YERWA c	1676	,,	,,	$10^{2.8}$
12	22-05-02/22-05-02	YERWA	EU1866	May 2003	,,	$10^{1.5}$
13	26-06-02/26- 06-02	YERWA	EU1863	May 2003	,,	$10^{2.8}$
14	18-02-02/18-02-02	SP d	1676	,,	,,	$10^{2.8}$
15	22-05-02/22-05-02	SP	EU1866	2003	,,	$10^{3.2}$

a = Epidemiological Unit, Borno State. (Storage). b = University of Maiduguri Teaching Hospital, Borno State. (Tertiary)

c = A Primary Health Centre in Borno State (Primary). d = Specialist Hospital (General Hospital, Borno State.) (Secondary

4. DISCUSSION

Failure to deliver at least one dose of measles vaccine to all infants aged 9 months, is attributed as the primary reason for this preventable morbidity and mortality. However, the issue to be concerned with should include, how many of the vaccinated children are actually immunized bearing in mind the poor conditions of storage and transportation of measles vaccines to vaccination centers in Africa with particular reference to Nigeria.

The findings of this study show high degree of primary vaccine failure (76%) with very low (12%) rate of seroconversion. It was also observed that pre-existing measles HI antibody (with GMT 36.6) grossly interfered with the vaccine, resulting in low post vaccination GMT of 22.9. The low sero-conversion rate could be multicausal as demonstrated by Onoja et al (1992), to include subpotency of the vaccines, improper handling of the vaccines during vaccination, storage of the vaccines etc. In this study it was observed that health workers in different Immunization centers improperly handled vaccines during vaccination. For instance most frozen ice packs used for keeping the vaccine at the beginning of a day's vaccination exercise were not changed even when they became hot later in the course of vaccination. In addition, it was observed most often that, the vaccine diluent was not stored at the same temperature as the vaccine before reconstitution. Such malpractice could adversely affect the potency of the vaccine. The corroboration of the finding of Onoja et al (1992) with this current study implies that there has been little or no improvement in the handling of measles vaccines in vaccination centres. Therefore adequate monitoring of vaccination exercise in each center should be enforced.

This study revealed that 85.7% of the mothers of the vaccinees tested had no measles antibody at the time of measles vaccination for their children. Probably not all the 16.9% of 136 vaccinees with pre-vaccination measles HI antibody were of maternal origin but due to natural infections. This speculation was supported by the fact that ten mothers whose children had pre existing measles antibody admitted that their children contracted clinical measles before they were brought for vaccination at the age of 9 months. The lack of maternal antibody among the majority of the vaccinees' mothers probably explains why many children in Northeastern Nigeria usually contract and occasionally die due to measles before the age of 9 months (the recommended age for measles vaccination in Nigeria). Contrary to this report, 94.25% of children at age 9-11 years in Southwestern Nigeria had no pre existing measles antibody (Onoja et al, 1992) and this probably explains the high rate of seroconversion recorded in that study. In this report about 78% of the vaccinated children were still found to be seronegative. The implication of this is that cohorts of susceptible children are at the risk of contracting and causing measles outbreak in their respective communities at the slightest exposure to measles virus. In our study, 5 mother-child pair had measles antibody at the age of 9 months while children of five seropositive mothers had none. But whether the antibody in the former group was of maternal origin is still uncertain. However, it is expected that women at child bearing age should have been exposed to subclinical measles at various stagse of life. Therefore, the low maternal antibody among the vaccinees' mothers observed in this study needs further evaluation. Nevertheless, a study 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 (Oyedele et al 2005). It is worth noting that these samples were collected in 2001/2002 when morbidity and mortality due to measles in Nigeria as a whole were very high. A report showed that, an overwhelming majority of the 561 deaths due to measles occurred in Northern part of Nigeria in 1999 (IRIN 2005). The high number of seronegative mothers and unimmunized children revealed in this study probably accounted for the menace caused by measles virus in northern Nigeria. In view of the observation in this study, when compared with that of Onoja et al, (1992), a parallel study of mother-child survey for measles antibody in both southern and northern Nigeria to ascertain the proper age at vaccination in Nigeria is suggested. Ensuring the quality of vaccines in terms of potency and cold-chain maintenance is very vital to the success of the Global measles vaccination Programme.

ACKNOWLEDGEMENTS

We wish to thank University of Maiduguri for supporting this project with a grant. Also, the technical assistance of David Bukbuk and management of UMTH is highly appreciated. We sincerely thank JICA for supplying the measles antigen through Dr Joshi

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Received: 8/2/2007

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