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Potency status and efficacy of measles vaccine administered in Nigeria: a case study of three EPI centres in Lagos, Nigeria.

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Summary

The potency status and efficacy of measles vaccines were studied in three immunization (EPI) centres in the suburban area of Lagos, Nigena. A total of 14 vials of measles vaccine were collected and subjected to potency testing while, 203 measles-vaccinated children were recruited for this study. Only 85 (41.87%) of the vaccinees reported back for the post-vaccination follow-up screening. The seroconversion pattern showed that 51(60%) had potent antibody titres ranging from 1:40 to 1:1280, while the remaining 34 (40%) had a low antibody titres between < 1:20 and 1:20. The vaccine potency test showed that only 1 (7.14%) of the 14 vaccine vials collected at these centres had virus titre of 3.5 Log while the remaining 13 (92.86%) had virus titres lower than 3.0 Log: the recommended human dose by the World Health Organisation (WHO) for measles vaccine. The administration of these subpotent and/or impotent vaccines vis-à-vis the status of immune response elicited in the vaccinees may be one of the reasons for the occurrence of measles infection in vaccinated children in the recent time in Nigeria. We herein suggested the subjection of all vaccines to a thorough standard laboratory screening before use in Nigeria.

Keywords: *Measles, vaccine, efficacy, potency, antibody.*

Résumé

L' immunogenicite et l'efficacite des vaccins contre la rougeole avaient ete etudiees dans 3 centres d'immunisation dans le sud de Lagos au Nigeria. Un total de 14 flacons de vaccin contre la rougeale avaient ete utilises pour tester l=immunogenicite, pendant que 203 enfants vaccines contre la rougeole avaient ete recrute's pour l'etude. 85 (41.87%) de vaccins sont revenus pour l'examen post vaccination. L.'examination du serum montrait que 51(60%) d'enfantsivaccines avaient des anticorps titres de 1:40 a 1:1280, pendant que le reste des 34 (40%) avaient unlitre d'anticorps moins eleve (titres varient entre< 1:20 et 1:20). Le teste d'immunogenicite a montre que 1(7,14%) seulement des flacons de vaccin pris dans les centres ont eu les virus titres de 3.5 log, pendant que le reste 13(92,86%) ont eu des titres de moins de 3.0 Log.' la dose recommandee a l'Organisation Mondiale de la Sante (OMS) pour le vaccin contre la rougeole. L' administration de quantite d'antigene inadquate pour stimuler la reponse du systeme immunitaire chez les vaccines peut etre l'une des raisons pour lesquelles la rougeole est encore observee chez les enfants vaccines aujour d'lue au Nigeria. Nous suggerons donc que toutles vaccins soeint par-paitement investiques par les laboratoires avant lew utilisation au Nigeria.

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Introduction

The main goal of most countries of the world is to control and completely eradicate vaccine-preventable childhood killer diseases of which measles is one. The strategy includes increasing the level of immunity in the age groups that are susceptible and/or, are at high risk to the disease [1,4] The introduction of the World Health Organisation's Expanded Programme on Immunization (WHO-EPI) and the administration of measles vaccine in most parts of the world in the last 3-decades have significantly reduced the global morbidity and mortality due to measles [1,5,7]. Despite the improved vaccine coverage globally in the recent years, measles still claims the lives of an estimated 1 million children a year, most of which occur in the developing countries [1].

The resurgence of measles, for instance, has highlighted concerns about United States programmes for immunization in infants and children [8]. Some African countries with high vaccine coverage levels have also reported measles outbreaks in children above the current target age group for immunization [9]. Measles resurgence has however been attributed to several factors including customs and strong traditional beliefs especially among mothers [10,11], but more importantly, the potency status of the measles vaccines as at the time of its administration [2,12,13]. The Nigeria-EPI, which was finally re-launched in 1984, recorded a high success in terms of vaccination coverage [11], but reports in the last 6-8 years show that measles is again on the increase, particularly in the vaccinated areas [14]. A laboratory backup service as suggested by Adu et al. [12] is thus important to provide more information on the vaccines and the levels of immunity conferred to the vaccinees after its administration. This study is meant to evaluate the potency status of measles vaccines administered in Lagos, Nigeria, and the level of protection it confers on children after vaccination.

Materials and methods

Study centres

Three government-owned primary health centres (PHC); Kajola Palm-Avenue and Isolo Road PHCs all situated in Mushin Local Government Area, a suburban area of Lagos state, were chosen as the study centres. The reported incidence of measles in this local government at the time of this study was high. Children brought to these centres were mainly from the lower and middle socioeconomic classes of the population.

Study population and sample collection

A total of 203 children, all aged 9 months attended these PHC between March and May, 1992 and who due for measles vaccination were recruited for this study. Seventy-six children were recruited in Palm-Avenue PHC, seventy-three from Kajola

PHC and fifty-four from Isolo road PHC. Pre-vaccination blood samples were collected from the children before the administration of the vaccine and the mothers were implored to bring their children back 4 weeks post-vaccination for further screening. The concepts of the study were explained to the mothers and their consent sought before blood samples were collected by thumb or heel puncture onto rectangular ROPACO filter paper as described by Nakano et al. [15]. All air-dried blood-soaked filter papers were stored away at 20 °C until used for serum extraction.

Measles vaccine potency test

Vials of measles vaccine administered at these centres during the period of this study were collected and their batch nos.,expiry date, and the date used for vaccination, were noted appropriately. All the vaccines were the lyophilised type obtained from UNICEF through the state EPI units. Aliquots of the reconstituted vaccines were collected immediately after rehydration at the vaccination centres and stored at 70°C until titrated for potency. Vaccine potency was determined on triplicate samples of confluent monolayer on Vero cells in 24-well tissue-culture plates according to WHO-guidelines. The cells were incubated at 37 °C and examined daily for 10 days. The virus end-point titre was calculated by the Reed and Muench method [16].

Haemagglutination inhibition (HI) test

All blood samples (pre- and post-vaccination) collected on ROPACO filter papers were warmed to room temperature, punched, treated, serum extracted and standardized to 1:10 as described by Nakano et al. [14]. The HI-test was performed as described by Munube [10]. In brief, two-fold serial dilution of sera were prepared from the 1:10 dilution obtained from the extraction. Prepared 4HA (Haemaglutinating) units per drop (25 µl) of commercially available measles antigen* was added to equal volume of each test sera and the plates incubated at 37 °C for 2 hours. A drop each of 0.5% monkey red blood cells was later added into the test and control wells and the plates further incubated at 25-28 °C (room temperature) for 1 hour.

Table 1: Measles HI-antibody distribution in vaccinees, 4 week post-vaccination at 3-EPI centres in Lagos, Nigeria

PHC* used as Study Cenres	Subjects: No. Bled Pre-vaccination	No. of returnees bled 4-week post vaccination (%)	HI-Antibody titres#: <1:20	1:20	1:40	1:80	1:160	1:320	1:640	1:1280	Total
Palm avenue	76	25(32.9)	3	-	-	1	3	3	1	14	25
Kajola	73	43(58.9)	26	4	3	1	2	2	3	2	43
Isolo road	54	17(31.5)	1	-	1	2	5	6	2	-	17
Total	203	85(41.9)	30	4	4	4	10	11	6	16	85

PHC = Primary Health Centre used for immunization programme. *#The Hi-antibody titres were determined 4 weeks post-vaccination*

Table 2: Profile of measles vaccines used at the three vaccination centres in Lagos, Nigeria.

S/No.	Date of vaccination	Vaccination centres	Batch no. of vaccine	Expiry date	Vaccine titre ($CCID_{50}$) per dose
1	26-3-92	Palm avenue PHC	4588-21	March '93	$10^{-3.5}$
2	30-4-92	Palm avenue PHC	4582-21	March '93	$<10^{-1}$
3	07-5-92	Palm avenue PHC	4582-21	March '93	$<10^{-1}$
4	14-5-92	Palm avenue PHC	4582-21	March '93	$10^{-2.25}$
5	04-3-92	Kajola PHC	M152 N11A	April '93	$<10^{-1}$
6	23-3-92	Kajola PHC	4582-21	March '93	$<10^{-1}$
7	30-3-92	Kajola PHC	4582-11	March '93	$<10^{-1}$
8	06-4-92	Kajola PHC	FLM 14-E269	April '93	$<10^{-1}$
9	18-5-92	Kajola PHC	A 152 NA 11A	April '93	$<10^{-1}$
10	18-5-92	Kajola PHC	MI 52 N11A	April ' 93	$<10^{-1}$
11	25-3-92	Isolo road PHC	4589-11	May '93	$<10^{-1}$
12	01-4-92	Isolo road PHC	4588-21	May '93	$<10^{-1}$
13	08-4-92	Isolo road PHC	4582-21	March '93	$<10^{-1}$
14	06-5-92	Isolo road PHC	4588-21	March '93	$<10^{-1}$

**Measles antigen manufactured by: Virion laboratory ltd., Ruuschlikon, Switzerland.*

Results

HI-test

All the 203 children screened pre-vaccination from the 3-PHC's had maternally derived measles HI-antibody titre range from 1:10 to 1:20. In all, only 85 (41.9%) of the 203 children bled pre-vaccination came back 4 weeks postvaccination for further screening: 25 (32.9%) of 76 bled from Palm-Avenue PHC; 43 (58.9%) of the 73 from Kajola PHC and only 17 (31.5%) of the 54 vaccinees from Isolo-Road PHC. The pattern of antibody distribution in vaccinees, post-measles vaccination screening at these centres are as shown in Table 1 and Figure 1. Briefly, 22 (88%), 13(30.2%), and 16(94.1%) from Palm-Avenue, Kajola, and Isolo-Road PHC's respectively had potent antibody titre ranges of 1:40 to 1:1280.

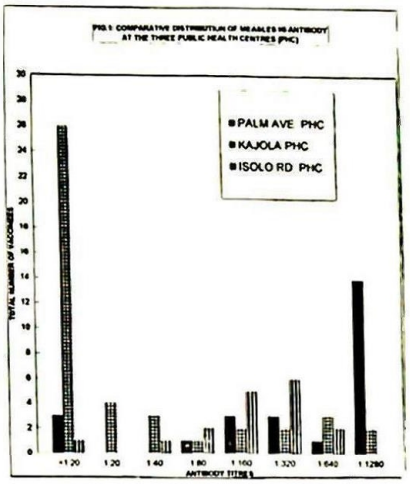

Fig. 1: Comparative distribution of measles Hi-antibody at the three primary health centres (PHC).

Vaccine potency test

The profile of the measles vaccines collected at the three centres with their titre values ($CCID_{50}$) per human dose is shown in Table 2. In brief, only 1 (7.14%) of the 14 vaccine vials tested from the 3-EPI centres met the WHO minimum standard requirement of 3 Logs per human dose.

Discussion

In Nigeria, one of the major problems facing studies on immunization monitoring, efficacy of vaccines and the level of immunity conferred on vaccinees, is the poor and nonchalant attitude coupled with traditional beliefs by individuals, especially mothers.

Our results on measles vaccine potency test is not encouraging as only one of the 14 vials (all from 7 batches) had virus titre value of 3.5 Log as against the titre range of <1.0 Log to 2.5 Log per dose recorded in the remaining 13 vaccine vials which is below the WHO minimum standard of 3.0Log ($1000CCID_{50}$) per human dose [17]. This observation is in agreement with the findings of Adu *et al.* [12] and Omilabu *et al.* [13], on separate studies on measles vaccines potency in Ibadan and Lagos, Nigeria, respectively. The loss in vaccine virus titres in Nigeria and other African countries have been attributed to the adverse environmental factors, poor handling by vaccinators, existence of chains of salesmen, lack of good storage system for vaccines, insensitivity to expiry date of vaccines and/or, administration of the expired vaccine [10,12,13,18,19]. Only Palm-Avenue, of the three EPI centres, had 1 (25%) of the 4 vials of measles vaccine used being potent with titre range of 2.5-3.5Log per human dose. This particular centre is the only one with adequate storage facilities, including a stand-by power generating set to augment the erratic public electric supply in the state. Little wonder then, that 22 (43.14%) of the 51 vaccinees who had protective measles HI-antibody titre range of 1:40 to 1:1280 were from this centre.

Out of the total 203 vaccines recruited for the study, only 85 (41.87%) came back for the 4 weeks postvaccination follow-up study. This observation usually, has been the pattern of vaccinees' response in Nigeria as reported by previous workers on low returns during postvaccination studies [12,14,19]. Of the 85 vaccinees that came back for the follow-up study, 51 (60%) developed protective measles HI-antibodies, titres ranging from 1:40 to 1:1280. This result is not too different from the findings of Adu *et al.* [12] in a separate study at Ibadan, Nigeria. The antibody response of the 60% vaccinees is however not high enough to adduce any reasonable inference of children's good pretection against measles and thus give a warning signal to our health-care system especially in a measles endemic country like Nigeria. The implication,thus,is that the unprotected 40% are at a high risk to the dreaded endemic wild measles virus attack and, possible spread may ensue due to re-exposure among the antibody-protected, thereby tasking and mopping-up their immunity until they finally succumb to the infection. This possibility is however yet to be confirmed by assessment of the immune status of children at specific periods (periodic check-up) as suggested by several workers in other measles endemic regions of the world. [12,15,20,21].

Our observation on the good antibody response by about 35% of vaccinees from Kajola and Isolo Road PHCs to these subpotent and/or impotent vaccines is strange, but remain for further investigation. The antibody response observed may however not be unconnected with the children's well-being and perhaps, their good nutritional status reflected in their healthy physical appearance during this study. It may also be that some of the children were given vitamin A supplements at their home postvaccination. Vitamin A has been found to be a potent immune enhancer and does not negatively interfere with vaccinees' response during immunisation [22-25].

In Nigeria, as well as other African countries, there were reports of incessant measles outbreaks, particularly, among already vaccinated [9,13]. Some of the factors attributed to be responsible and promoting this include: administration of subpotent and/or impotent expired vaccine, high level of malnutrition, low level of vitamin A intake, lack of adequate case management, non-availability of storage facilities for vaccines and lack of laboratory backup potency testing for the imported measles vaccines used for immunization programmes [10,12-15,24,26,27]. We therefore suggest the subjection of vaccines, through random sample, used for immunization programmes to a thorough standard laboratory check-up before use in Nigeria.

The increase in measles epidemics in recent years may be a warning sign of problems with our system of primary health care and vaccination policies in Nigeria. Attempts towards the isolation of the wild strains of measles virus and its use in the development of a heat stable vaccine in Nigeria is an open area of research already being explored and may generate data and/or information that will assist in the eradication of measles in Nigeria.

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