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Neutralization Antibodies in Oral Poliovirus Vaccine (OPV) Vaccinated Children and Young Adult in Bida North Central, Nigeria

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Abstract - Following the widespread use of Poliovirus Vaccine in the mid-1950s, the incidence of poliomyelitis declined rapidly in many industrialized countries. While now rare in the western world, Polio is still endemic to South Asia and Nigeria. This is no doubt a burden to the Federal Government of Nigeria. This work studied the serological response of OPV trivalent formulation in order to observe the Seroconversion rate among the OPV recipients in Bida, Niger State North Central Nigeria using Neutralization Method. Samples were collected from 200 children and young adults that have been immunized with Oral Poliovirus Vaccine in Bida community. Participants are within the 1st day to 15 years of age. There was no significant statistical difference between poliovirus serotypes and sex ($P > 0.05$). It was observed that 60% of the 5 neonates (age less than 4 weeks) that participated in the study with zero dose or first dose has antibody titer level> 1:8 for more than two poliovirus serotypes, while 57.14 % of the 7 infants less than 10 weeks (< 3 months) has protective antibody titer level > 1:8 for more than two poliovirus serotypes. The responsiveness against poliovirus vaccine varied much between children at different ages. It was observed that there were low mean titer values for the three serotypes in age group 5.1 -10years and 10.1 – 15years compared to age groups below5years. It was also discovered that some of the studied cases have no protective level of antibodies which represent a high risk factor if they are exposed to clinical doses of wild poliovirus with seronegativity rates for PV1=43.68%, PV2=45.37%, PV3=44.07%. Therefore, it is recommended that indigenous vaccine production, repeat vaccination among children below5 years and measurement of protective antibodies against poliovirus at different intervals to ascertain both the immune status of the vaccine recipients and the validity of the vaccine, be encouraged.

Keywords - Neutralization antibodies, OPV, Children, Young Adults, Bida-Nigeria

1. Introduction

Poliomyelitis, often called polio or infantile paralysis, is an acute viral infectious disease spread from person to person, primarily via the fecal-oral route (Cohen, 2004). The term derives from the Greek polios, meaning, “grey”, myelos, referring to the “spinal cord”, and the suffix –itis which denotes inflammation. (Chamberlin and Narins 2005). Although about 90% of polio infection causes no symptoms at all, affected individuals can exhibit a range of symptoms if the virus enters the blood stream (Ryan and Ray, 2004). In about 1% of cases, the virus enters the central nervous system, preferentially infecting and destroying motor neurons leading to muscle weakness and acute flaccid paralysis. Different types of paralysis may occur depending on the nerves involved. Spinal Polio is the most common form, characterized by asymmetric paralysis that most often involves the legs. Bulbar polio leads to weakness of muscles innervated by cranial nerves. Bulbospinal polio is the combination of bulbar and spinal paralysis (Atkinson *et al*, 2007).

Poliomyelitis was first recognized as a distinct condition by Jacob Hein in 1840, in1908 poliovirus was identified by

Karl Landsteiner as the causative agent of poliomyelitis (Paul, 1971). Although major polio epidemics were unknown before the late 19th century, polio was one of the most dreaded childhood diseases of the 20th century. Polio epidemics have crippled thousands of people mostly young children; the disease has caused paralysis and death for much of human history. Polio had existed for thousands of years quietly as an endemic pathogen until the 1880s, when major epidemics began to occur in Europe; soon after, widespread epidemics appeared in the United States (Trevelyan *et al*, 2005).By 1910, much of the world experienced a dramatic increase in polio cases and frequent epidemics became regular events, primarily in cities during the summer months. These epidemics which left thousands of children and adult paralyzed provided the impetus for a "Great Race" towards the development of a vaccine. Polio vaccines are developed in 1950s and are credited with reducing the global number of polio cases per year from many hundreds of thousands to around a thousand (Aylward, 2006). Enhanced vaccination efforts led by the World Health Organization, UNICEF, and Rotary International could result in global eradication of the disease (Heymann, 2006).

In all countries, children under two years of age create a microenvironment of less than optimal hygiene within the family and within daycare settings, readily facilitating feacal-oral and oral-oral (mouth-fingers-mouth) transmission. Feaces can serve as a source of contamination of water, milk, or food and housefly can passively transfer poliovirus from feaces to food (Gear, 1952)

It has been reported that there is an association between paralysis of a limb due to poliomyelitis and receipt of an injection of DPT vaccine in the limb during the preceding 30 days (McCloskey, 1950, Sutter *et al 1992*). These cases are usually reported in children 6 months of age or older, reflecting the fact that most infants are protected from poliomyelitis during the first few months of life by maternal antibodies. As maternal antibody titres wane, susceptibility increases. Therefore, it is desirable to complete a primary series of OPV/DPT immunization by 4 months of age, during which time the risk of post-injection poliomyelitis is extremely low.

This study was carried out to advocate for policy formulation that will encourage measuring the protective antibodies against polioviruses at different intervals to check the validity of the used vaccine and if need be to support repeat vaccination, observe the level of antibody against OPV at different age groups and to advocate for zero dose for OPV in new born by measuring the level of antibodies using serum neutralizing antibodies method.

2. Materials and Method

The study is a descriptive cross-sectional study that was carried out in Federal Medical Centre Bida and General Hospital Bida, Niger State. Samples of patients that visited the hospitals for the purpose of immunization that were referred for laboratory investigations in Hematological test such as PCV ,Blood Group and Genotype were recruited into this study. The inclusion criteria were age, 1st day – 15 years, sex; male and female and apparently healthy children.

Informed consent was obtained from parents and a well-structured questionnaire was administered to capture all relevant bio - data of participants.

The total sample size for this study was 200, the simple random sampling method was applied where the subjects from the target population with equal probability of selection for a study power of 95%.

Two to three milliliters of whole blood sample was collected from each subject into a plain tube, and then processed into serum by centrifugation at 3,000 revolution per minute for 5 minutes and were stored at -20^{0}C until the test .To maintain cold chain in order to preserve the antibodies present, isothermal packaging boxes with ice packs were used to transport the samples to the laboratory.

2.1. Measurement of Serum Neutralizing Antibody

The frozen sera were thawed at room temperature (25^{0}C) for 45minutes, samples were mixed, test for serum neutralizing antibodies are considered to be the most specific for determining the protective antibody response to poliovirus infections, and was used in this study because it allows differentiation between antibodies to wild or vaccine strains. Sample analysis was carried out in the University of Maiduguri Teaching Hospital Reference Polio Laboratory Maiduguri Bornu State, Nigeria.

3. Statistical Analysis

The data generated from this study was entered using SPSS statistical package version 15.0 for the analysis. Descriptive statistics was used to explain the frequency distribution while T-test and ANOVA was used to test the significant different among the titer levels at P= 0.05.

4. Results

Two hundred participants' samples were collected from children and young adults among population of children immunized and infants (less than a day old) not yet immunized in Bida. The participants in this study are male and female, 52.5% are male while 47.5% are female, within the ages of less than 1 day – 15 years. Out of these 200 participants, 3.5% are between <1day – 30 days, while 1 – 6months constitutes 4% , 6.1months-1year constitutes 10%, 1.1years – 2years were 9.5%, 2.1years -5years constitutes 18.5%, 5.1years -10years is 37 % and 10.1years-15 years were 17.5%.Majority of the participants (37%) fall within age group 5.1years -10 years while the least participants(3.5%) fall within <1 day- 30days follow by 1 month – 6 months(4%) as shown in **Table I.**

Table I. Age group frequency distribution table

Age group	Frequency	Percent
0-30 days	7	3.5
31days-6months	8	4.0
6.1months-1years	20	10.0
1.1years-2years	19	9.5
2.1years-5years	37	18.5
5.1years-10years	74	37.0
10.1years-15years	35	17.5
Total	200	100

Table II (a) showed the Seroconversion rate of the trivalent OPV used in Bida community , out of 200 participants samples screened for the presence of neutralizing antibodies to poliovirus, 68.5%,66.5% and 66% seroconverting rate were observed for PV1, PV2 and PV3 respectively. Of these seropositive cases the highest mean titer of 97.14 for PV1 recorded were in the age group 6.1months-1year followed by 76.21 in age group 1.1years-2years, 73.71 in 0-6months, 65.08 in 2.1years -5years while mean titers 37.24, 18.51 were observed in age group 5.1years -10years and 10.1years – 15years respectively. The highest mean titers of 70.67 was observed for PV2 in age group 6.1 months- 1year, followed by 50.74 in 1.1years-2years, 40.03 in 2.1years – 5 years, 27.71 in 0-6months while lowest mean titres of 25.46 and 19.66 were observed in age group 5.1years -10years and 10.1years -15years respectively. The highest mean titers of 106.11 was observed for PV3 in age group 1.1years -2years, followed by 105.9 in 6.1months – 1 year, 96.57 in 0 – 6months , 72.00 in 2.1years -5years while 46.16 and 36.91 were observed in age group 5.1years-10years and 10.1years -15years respectively in **Table II.**

Table II (a). Seroconversion rates among the study population.

SEROCONVERSION	No	PV 1 (%)	PV 2 (%)	PV 3 (%)
SEROPSITIVITY	200	68.5	66.5	66.0
SERONEGATIVITY	200	31.5	33.5	34.0

Table II. Seroconversion rates among the study subjects for the three serotypes.

Age group	N	PV1 (%)	PV2 (%)	PV3 (%)
0 - 6months	14	42.9	35.7	42.9
6.1months-1year	21	66.7	61.9	76.2
1.1years-2years	19	57.9	73.7	52.6
2years-5years	37	62.2	64.9	62.2
5years-10years	74	56.8	45.9	44.6
10.1years-15years	35	51.4	45.7	57.1

There were significant statistical difference (P<0.05) in mean titer for PV1 (P value = 0.006) and PV3 (P value=0.024) relative to age while there was no significant statistical difference in mean titers for PV2 (P value=0.075) relative to age in Bida as shown in **Table III.**

Table III. Mean titers of poliovirus serotypes by age distribution.

AGE GROUP	N	PV1(Mean titre)	PV2(Mean titre)	PV3(Mean titre)
0-6months	14	73.71	27.71	96.57
6.1months-1year	21	97.14	70.67	105.90
1.1years-2years	19	76.21	50.74	106.11
2.1years-5years	37	65.08	40.03	72.00
5.1years-10years	74	37.24	25.46	46.16
10.1years-15years	35	18.51	19.66	36.91

Anova

PV1	PV2	PV3
0.006	0.075	0.024

Table**IV** showed comparison of PV1, PV2 and PV3 by sex. Male had the highest mean titer of 96.00 for PV1 in age group 6.1months - 1year, 101.71 in the same age group for PV2 while the highest mean titre of 192.00 for PV3 was recorded in age group 0-30days.The lowest mean titre for PV1, PV2 and PV3 in Male were; 24.00, 12.00, and 14.40 in 10.1years - 15years, 0-30days, and 31days-6months respectively. The P values of Male for PV1 = 0.530, PV2 = 0.008 and PV3 = 0.579.

Table IV. Mean titers for serotypes by Male age groups

AGE GROUP	N	PV1	PV2	PV3
0-30days	3	64.00	12.00	192.00
31days-6months	5	57.60	19.20	14.40
6.1months-1years	7	96.00	101.71	125.71
1.1years-2years	11	37.82	49.09	124.36
2.1years-5years	23	86.61	39.35	66.61
5.1years-10years	37	37.73	24.43	68.76
10.1years-15years	19	24.00	25.90	52.42

Anova

PV1	PV2	PV3
0.530	0.008	0.579

Table V showed that Female had the highest mean titer of 130.00 for PV1 in 0-30 days, 59.38 in 6.1months-1year for PV2 and 144.00 in 0-30 days for PV3 while the lowest mean titer of 12.00, 0.00 and 18.59 forPV1, PV2 and PV3 were observed in 10.1years -15years, 31days-6months, and 10.1years- 15 years respectively in female. The P values for PV1= 0.006, PV2= 0.075 and PV3=0.024. There were significant statistical difference in comparison of poliovirus serotypes and sex (Male) for PV1 and PV3 while there was no significant statistical difference in PV2**.**

Table V. Mean titers for serotypes by Female age groups

AGE GRP	N	PV1	PV2	PV3
0-30 days	4	130.00	64.00	144.00
31days-6months	3	10.67	0.00	42.67
6.1months-1year	13	105.23	59.38	103.38
1.1years-2years	8	129.00	53.00	81.00
2.1years-5years	14	29.71	41.14	80.86
5.1years-10years	37	36.76	26.49	23.57
10.1years-15years	16	12.00	12.25	18.59

Anova

PV1	PV2	PV3
0.006	0.075	0.024

5. Discussion

In 1996, polio was rampant in at least 41 African countries. Tragically, as many as 75,000 African children were paralyzed every year. Since then tremendous progress has been made towards eradicating polio from Nigeria. In fact, until 2002, many states in the south of Nigeria were largely polio-free. World Health Organization is committed to ensuring that the Federal Government fulfills her goal of stopping poliovirus transmission in Nigeria (WHO, 2011).

In the generic sense, vaccination works by priming the immune system with an 'immunogen' stimulating immune response, via use of an infectious agent, is known as immunization. Vaccine efficacy is defined by the amount of immunity a particular vaccine provides against infection, and is often measured by detection of protective antibodies in the blood (Fedson, 1998).

The development of immunity to polio efficiently blocks person-to-person transmission of wild poliovirus, thereby protecting both individual vaccine recipients and the wider community. Because there is no long-term carrier state for poliovirus in immunocompetent individuals, polioviruses have no non-primate reservoir in nature, and survival of the virus in the environment for an extended period appears to be remote, interruption of person-to- person transmission of the virus by vaccination is the critical step in global polio eradication (Fine and Carneiro, 1999).

The scientific strategy of any immunization program is to secure protection before infants are at risk of developing a disease. In developing countries the majority of cases of paralytic poliomyelitis reported in outbreaks, occur in children under 5 years of age (WHO, 1993). Both the community based and hospital based data, in polio endemic areas show that more than three quarters of the paralytic cases occur in children younger than 2 years of age (Onadeko and Familusi, 1990). In developing countries, microbial flora colonized a child's intestine and in order to avoid possible interference, administration of OPV very early in life is important. This was the basis for WHO recommendation that a zero dose should be administered during the neonatal period to children in all poliomyelitis endemic countries (EPI, 1985). The importance of providing vaccine as early in life as possible before exposure to wild virus occurs cannot be over emphasized.

In this study out of 200 participants, only 7(3.5%) were within less than a day -30days , 8(4%) were within 1 month-6months,20 were within 6.1 months-1 year while 19 were within 1.1years-2years . Out of all the participants, the minimum mean antibody titres were 18.51 for PV1, 19.66 for PV2 and 36.91 for PV3 and these were observed in the age group 10.1years-15years, which represents the young adults. Halsey and Galazka, in 1985 remarked that if the titre obtained after immunization is fourfold rise in neutralizing antibody titre or a change from seronegativity to seropositivity, it is concluded that the recipient has responded to the vaccine.

The minimum mean antibody titre observed is greater than fourfold rise (1:8) 10years – 15 years after immunization supports the claim of Sabin and Boulgar (1973), that OPV provides long lasting immunity. The maximum mean antibody titre observed were PV1=97.14 age group 6.1months-1year, PV2=70.67 age group 6.1months-1year and PV3=106.11 age group 1.1years-2years, these age groups represents the infant group. This observation is similar to the study conducted in China, a higher percentage of infants fed with a dose of OPV at birth had serum antibodies against the three types of poliovirus in their younger age (Dexiang, 1986).In Brazil and in India, serological responses were also good in infants after immunization with OPV.

Halsey and Galazka found that among neonates who received a dose of OPV, 30 – 50 % developed serum antibodies to one or more poliovirus serotypes (Halsey and Galazka, 1985). Zero dose are administered at birth or within the first four weeks of life, in Bida community the study revealed a response between 35.7% to 42.9 %, this finding is closely similar to that of Halsey and Galaska. A single dose of oral polio vaccine produces immunity to all three poliovirus serotypes in approximately 50% of recipients (Atkinson et al, 2007). While three doses of live-attenuated OPV produce protective antibody to all three poliovirus types in more than 95% of recipients. In Bida it was observed that more than three doses produced averagely 54.63% to 56.32% in the study subjects which is apparently lower than Atkinson et al. findings, and America Academy of Pediatrics committee on infectious Disease 1997, that OPV produces excellent immunity in the intestine, the primary site of wild poliovirus entry, which helps prevent infection with wild virus in areas where the virus is endemic.

In this study there was close variation in the percentage of children seroconversion with a rate of 56.32% for serotype 1, 54.63% for serotype 2 and 55.93% for serotype 3,(Table II) this is at variance with the previous studies conducted in 15 developing countries, where wide variation in the percentage of children seroconversion rates of 73% for type 1, 90% for type 2 and 70% for type 3 were reported (Patriarca, 1991) and also differ from that of American Academy of Pediatrics Committee on Infectious Diseases that more than 95% of OPV recipients produced protective antibody to all poliovirus serotypes. Less optimal response to trivalent OPV was observed in Bida just as it was reported to have begun to appear in medical literature as far back as 1970 in developing countries as a result of low rates of seroconversion to poliovirus type 1 and 3(Ghosh , 1970; John and Jayabal, 1972; Oduntan et al., 1978).

It was observed in this study the relationship between the production of protective antibody against the three serotypes in male age groups (Table IV) and female age groups (Table V). It was found that the mean titers of male and female children between age group 1st days – 30 days is high enough and this is referred to as maternal antibody where during the first few months of life most infants have circulating IgG antibody acquired from the mother before birth. It was also observed that the neutralizing antibody titers recorded in the female are more than the male as observed in most of the age groups indicating that the female subject elicit more immune response to OPV (Table IV and V).

The age groups 2.1years to 5years shows a significant increase in the antibody titers of greater than 40 for the three serotypes while antibody titer levels dropped below 46 in the age group > 5 years to 15 years. (Table III). There is significant statistical difference ($P<0.05$) in mean titer for PV1 and PV3 relative to age while there is no significant statistical difference in mean titer for PV2.($P > 0.05$).

6. Conclusion

The study assessed the level of protective antibody titer against poliovirus among the children receiving Oral Poliovirus Vaccine and young adult living in Bida community Niger State North Central Nigeria. The possible high risk of infection of neonates with wild poliovirus as observed in the study may be due to absence of effective strategies to adhere to Global Advisory Group. It could also be because of low-adherence to WHO guidelines on poliovirus global eradication to ensure zero dosage of OPV at birth. The Federal Government must pay more attention to other factors that undermine the efficacy and effectiveness of the vaccine in the recipients in order to stop poliovirus transmission in Nigeria.

Seroconversion rates of 56.32% were found for PV1, 54.63% for PV2 and 55.93% for PV3 in the study population. In the light of the above finding, consideration should be given to conduct further studies to compare the efficacy of monovalent OPV to any of the serotypes in Bida community.

In view of the substantial burden of poliomyelitis in only six countries of the world, including Nigeria, the Federal Government must put in more effort to strengthen structures that support accessibility of the vaccine in every locality. The Government must encourage administration of globally accepted key strategies at all levels of healthcare to combat poliovirus transmission in Nigeria.

Our findings support the needs to ascertain the effectiveness of the OPV at each vaccination schedule in Bida by collaborating with Bida Local government Primary Health Care department. Moreover, the compliance of immunization officer on the adherence to international best practice for transportation of the vaccine to the field by ensuring the availability of cold chain facilities is a concern. In addition, checking vaccine recipient for serum neutralizing antibody against all the poliovirus serotypes for possible repeat of vaccination will serve as an intervention to reducing the burden of poliomyelitis infection and its eradication in Nigeria.

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