ORAL POLIO VACCINE STATUS AND OCCURENCE OF WILD POLIO VIRUS AMONG REPORTED ACUTE FLACCID PARALYZED CHILDREN IN NIGERIA.

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CERTIFICATION

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DEDICATION

I dedicate this project to the Lord God Almighty, my parents and my husband.

ACKNOWLEDGEMENT

ABSTRACT

Nigeria remains one out of the three countries in the world yet to interrupt endemic Poliomyelitis. The disease thus continues to thrive in Nigeria, Afghanistan and Pakistan. Four doses of OPV have been used in the Polio Eradication Initiative Programme in Nigeria. However, a single dose of Oral Polio Vaccine has been known to produce immunity to approximately 50% of recipients and three doses to 95%. Thus multiple Immunization Campaigns have been carried out and yet there is failure to eradicate Poliomyelitis. This failure to eradicate the disease globally raises the question of the effectiveness of the continuing use of 4 doses of OPV in the prevention programme in endemic Countries. Understanding the association between the Oral Polio vaccine Status and Wild Poliovirus cases among AFP cases could help provide details for policy direction on the number of OPV to be given during Campaigns. This study was therefore conducted to determine the optimum OPV dose for prevention of Wild Poliovirus in Nigeria and its Clinical Effectiveness under field conditions in the actual community

Secondary data analysis from 2009 to 2012 of the National AFP Surveillance System from the 36 states and FCT in Nigeria was done. Descriptive statistics was used to describe AFP occurrence. OR and ROC curve was used to determine the clinical effectiveness of OPV and logistic regression used to identify predictors of the disease.

A total of 24848 cases of AFP were analyzed. About half were between 12-35 months of age with 57% males. Northern states had the highest occurrence of AFP cases reported (29%).A majority (70.7%) had received over 3 doses. Efficacy of OPV was found to be maximized in children who had received 4 doses (92%) followed by 80% in those with 3 doses and 57% in those with 2 doses.OPV sensitivity and specificity was maximum at a cut-off point of 4 doses producing the best efficacy on the ROC curve.

It is therefore recommended that 4 doses of OPV should be continued in the National Polio Eradication Programme. **Keywords:**

Poliomyelitis , Oral Polio vaccine, Receiver Operating Characteristic Curve and Clinical effectiveness of Oral Polio vaccine

336 words

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LIST OF ABBREVIATIONS

PV: Poliovirus

WHO: World Health Organization

CDC: Centres for Disease Control

AFP: Acute Flaccid Paralysis

OPV: Oral Polio Vaccine

WPV: Wild Polio Virus

GPEI: Global Polio Eradication Initiative

UNICEF: United Nations Children Education Trust Funds

VE: Vaccine Effectiveness

ROC: Receiver Operating Characteristic

NC: North Central

NE: North East

NW: North West

SE: South East

SS: South South

SE: South East

SD: Standard Deviation

SPSS: Statistical Package for Social Sciences

CHAPTER ONE

INTRODUCTION

1.1 General Background

Polio or Poliomyelitis is an acute viral disease characterized by inflammation of the nerve cells of the brain stem and the spinal cord. The disease is caused by a virus called Poliovirus. It belongs to the genus, Enterovirus and the family, Picornaviridae. Viruses in this family are small in size with single stranded RNA. There are 3 serotypes: types 1, 2 and 3. Type 1 is the commonest and most virulent. Type 2 has not been detected globally since 1999. (Hovi et al, 2001).

Most cases are seen during the hot humid months, with the virus infecting all susceptible individuals (Nathanson et al, 1984) Paralysis is seen in about 1% of all infections. Transmission usually occurs via the fecal-oral route (Plotkin et al, 2008). Immunity against polio is conferred through immunization or natural infection, with immunity to one type not necessarily resulting in immunity to the remaining two types. (Plotkin et al, 2008) Achieving vaccine-induced immunity requires at least three doses of OPV, and even a higher number of doses through mass vaccination campaigns in endemic countries such as Nigeria, where persistent circulation of the virus has never been interrupted ((Plotkin et al, 2008) (WHO, 2008). With model polio vaccination campaigns in the Americas in the last half of the 20 th century resulting in the interruption of wild poliovirus circulation in that region, the WHO (World Health Assembly, 1988) launched a global effort to eradicate polio.

In May 2012, after more than 20 years of mass vaccination campaigns, the 65th World Health Assembly declared that the completion of poliomyelitis eradication was a "programmatic emergency for global public health". (WHA, 2012) A lot of progress has been made with the initiation of Global Polio Eradication Initiative. The four key strategies outlined by the World Health Organization for stopping polio transmission are:

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- High infant immunization coverage with four doses of oral polio vaccine (OPV) in the first year of life in developing and endemic countries, and routine immunization with OPV and/or IPV elsewhere.

- Organization of "National immunization days" to provide supplementary doses of oral polio vaccine to all children less than five years of age.

- Active surveillance for wild poliovirus through reporting and laboratory testing of all cases of acute flaccid paralysis among children less than fifteen years of age.

- Targeted "mop-up" campaigns once wild poliovirus transmission is limited to a specific focal area.

Substantial financial and political pledges to poliomyelitis eradication have recently re - intensified efforts, and prevalence of poliomyelitis is at a historical low level, although transmission in Afghanistan, Pakistan, and Nigeria remains persistent. Globally, case numbers have fallen (1651 cases in 2008 *vs* 223 in 2012), and India, once one of the most entrenched reservoirs, is now free of indigenous poliovirus transmission. However, in Nigeria, Poliomyelitis cases doubled between 2011 and 2012, with sustained transmission of all three serotypes in 2012 (103 and 19 cases due to serotypes 1 and 3 wild poliovirus and eight due to circulating vaccine-derived poliovirus type 2 [cVDPV2]). In 2012, Nigeria was the global epicenter of poliovirus outbreaks, astonishing those who commended its success during 2010 when case numbers fell by 95%. (WHO, Meeting of the Strategic advisory group of experts on immunization, November 2011, 2012)

1.2 Problem Statement

The number of polio cases has fallen by 99% since 1988(350,000 cases to 650 in 2011.) 125 countries were endemic in 1988 as compared to 3 Countries in 2014. The failure to stop Polio in the remaining areas could result in as many as 200,000 new cases every year, within 10 years all over the world. At present there are 3 endemic countries remaining in the world: Afghanistan, Pakistan and Nigeria (WHA, 2012). Nigeria constitutes 95% of the total WPV in the World (100% to Polio burden in Africa) & only Country where the 3 serotypes exist; WPV1&3 and cVDPV2) despite several campaigns. Nigeria can be said to hold the key to Polio eradication in Africa and possibly the whole world.(Mangal et al, 2014) In 2012 there were 122 cases of Wild

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Polio Viruses in Nigeria- (223 globally), 90% in the North and 16 WPV cases in 2013- (CDC, 2013). Children that took as many as 20 doses of OPV are known to be infected with Wild Polio Virus.

In 2012, 77% of the children who took many doses of OPV still came down with WPV – (WHA, 2012). Nigeria is so slow in eradication of Wild poliovirus as a result of many factors including bad politics, refusal of the OPV, bad health system. There is therefore need to find out the optimum OPV dose that will help prevent occurrence of Poliomyelitis in Nigeria.

1.3   Justification

It is a known fact that Poliomyelitis is endemic in Nigeria despite the fact that 4 doses of the Oral Polio vaccine is routinely given to children. The thriving of Wild Poliovirus in Nigeria poses a serious threat to the eradication of Poliomyelitis globally as Viruses from Nigeria can be imported and continue to cause epidemics in other nearby countries due to hidden or reestablished transmission (WHA, 2012).

Poliomyelitis therefore has to be eradicated globally. The eradication of Poliomyelitis has been declared as an emergency. With four doses being given routinely and yet the continued spread of the Poliovirus, it is possible that 4 doses are not sufficient for the prevention of the disease.

Other socio-demographic factors may also be associated with the continued occurrence of the disease and there is also the possibility of reduced clinical effectiveness of the Oral Polio vaccine under field condition in the actual community. It is worthy to note that the Set date for eradication has been fixed a number of times and it is unknown when eradication will be achieved.

As earlier stated, despite many OPV doses (on-going efforts) given, children who receive this vaccine are still contracting the wild Poliovirus infection. There is therefore the need to know how many OPV doses a child should be given that will have protective effect. Use of epidemiologic technique to predict this optimum dose is therefore highly indicated.

Findings from this study will indicate and provide the optimum OPV dose that will prevent the occurrence of Poliomyelitis crucial to the achievement of eradication and determine clinical

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effectiveness of the OPV in Nigeria. This study will provide findings that will advise ~~Program~~ managers and Clinicians appropriately as well as guide policy makers.

1.4 Research Questions

This study will answer the following questions:

1. What is the Pattern of Acute Flaccid paralysis (AFP) reported and investigated in the National Polio Surveillance System?

2. What is the Oral Polio Vaccine (OPV) Status of the AFP cases in Nigeria?

3. What is the Epidemiology of Wild Poliovirus (WPV) isolated in the national Polio Surveillance System by sex, number of dose of OPV taken, location, age and trends over ~~time~~ ?.

4. How the dose of OPV and socio-demographic factors are associated with occurrence of Wild Polio Virus among AFP cases?

5. What is the Optimum dose of OPV that is needed to prevent the occurrence of Wild Polio Virus?

1.5 Objectives

Broad Objectives:

To describe the Epidemiology of Wild Poliovirus and determine the optimum dose of OPV needed to prevent its occurrence among reported AFP cases using the National AFP Surveillance System Data.

Specific Objectives:

1. To determine the Pattern of Acute Flaccid paralysis (AFP) reported and investigated in the National Polio Surveillance System.

2. To assess the Oral Polio Vaccine (OPV) Status of the AFP cases and WPV cases.

3. To describe the Epidemiology of Wild Poliovirus (WPV) isolated in the national Polio Surveillance System.

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4. To determine the clinical effectiveness of Oral Polio vaccine.

5. To identify the socio-demographic factors and dose of OPV associated with occurrence of WPV.

6. To predict the Optimum dose of OPV that is needed to prevent the occurrence of Wild Polio Virus.

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CHAPTER TWO

LITERATURE REVIEW

2.1 Definition of Poliomyelitis

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 et al, 2004) The term derives from the Ancient Greek *poliós* (πολιός), meaning "grey", *myelós* (μυελός "marrow"), referring to the grey matter of the spinal cord, and the suffix *-itis*, which denotes inflammation. (Chamberlin et al, 2005). It is the effect of the Poliomyelitis virus on the spinal cord that leads to the classic manifestation; paralysis.

Although approximately 90% of polio infections cause no symptoms at all, affected individuals can exhibit a range of symptoms if the virus enters the blood stream. (Ryan et al, 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 a combination of bulbar and spinal paralysis. (Atkinson et al, 2009)

Poliomyelitis is caused by infection with a member of the genus *Enterovirus* known as poliovirus (PV). This group of RNA viruses colonize the gastrointestinal tract (Cohen, 2004) — specifically the oropharynx and the intestine. The incubation time (to the first signs and symptoms) ranges from three to 35 days, with a more common span of six to 20 days. PV infects and causes disease in humans alone. Its structure is very simple, composed of a single (+) sense RNA genome enclosed in a protein shell called a capsid. (Atkinson et al, 2009) Three serotypes of poliovirus have been identified—poliovirus type 1 (PV1), type 2 (PV2), and type 3 (PV3)—each with a slightly different capsid protein. (Katz et al) All three are extremely virulent and produce the same disease symptoms. PV1 is the most commonly encountered form, and the one most closely associated with paralysis. (Ohri et al, 1999).

CHAPTER TWO

LITERATURE REVIEW

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The virus does not survive long in the environment outside the human body and there is no long-term carrier state. Person -to --Person spread via faeco-oral route is the most important route of transmission. Oral-oral route may also account for some cases. Two peaks of transmission, February to May (low transmission period) and August to November (high transmission period) in Africa are recognized, while transmission peaks in winter in the temperate countries. Cases are most infectious from 7 to 10days before and after the onset of symptoms (Atkinson et al, 2009)

2.2 History of Poliomyelitis

Poliomyelitis was first recognized as a distinct condition by Jakob Heine in 1840. Its causative agent, poliovirus, was identified in 1908 by Karl Landsteiner (Nathanson et al, 1984,Paul, 1971)Polio had existed for thousands of years in certain areas, with depictions of the disease in ancient art. Major polio epidemics started to appear in the late 19th century in Europe and soon after the United States ,(Trevelyan et al, 2005)and it became one of the most dreaded childhood diseases of the 20th century. Developed in the 1950s, polio vaccines have reduced the global number of polio cases per year from many hundreds of thousands to under a thousand today through enhanced vaccination efforts led by Rotary International, the World Health Organization, and UNICEF which should result in global eradication of the disease

2.3 Diagnosis of Poliomyelitis

If poliovirus is isolated from a patient experiencing acute flaccid paralysis, it is further tested through oligonucleotide mapping (genetic fingerprinting), or more recently by PCR amplification, to determine whether it is "wild type" (that is, the virus encountered in nature) or "vaccine type" (derived from a strain of poliovirus used to produce polio vaccine) .(Chezzi, 1996) It is important to determine the source of the virus because for each reported case of paralytic polio caused by wild poliovirus, an estimated 200 to 3,000 other contagious asymptomatic carriers exist. (Gwande, 2004)

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2.4   Prevention using vaccination

Two types of vaccine are used throughout the world to combat polio. Both types induce immunity to polio, efficiently blocking person-to-person transmission of wild poliovirus, thereby protecting both individual vaccine recipients and the wider community (so-called herd immunity). (Carneiro, 1999)

The first candidate polio vaccine, based on one serotype of a live but attenuated (weakened) virus, was developed by the virologist Hilary Koprowski. Koprowski's prototype vaccine was given to an eight-year-old boy on February 27, 1950 .(Koproski, 2010) Koprowski continued to work on the vaccine throughout the 1950s, leading to large-scale trials in the then Belgian Congo and the vaccination of seven million children in Poland against serotypes PV1 and PV3 between 1958 and 1960. (Koproski, 2010)

The second inactivated virus vaccine was developed in 1952 by Jonas Salk at the University of Pittsburgh, and announced to the world on April 12, 1955. (Spice, 2005) After two doses of IPV (given by injection), 90% or more of individuals develop protective antibody to all three serotypes of poliovirus, and at least 99% are immune to poliovirus following three doses. (Atkinson et al, 2009)

2.5   Oral Polio Vaccine

Subsequently, Albert Sabin developed another live, oral polio vaccine (OPV). It was produced by the repeated passage of the virus through nonhuman cells at subphysiological temperatures. The attenuated poliovirus in the Sabin vaccine replicates very efficiently in the gut, the primary site of wild poliovirus infection and replication, but the vaccine strain is unable to replicate efficiently within nervous tissue. (Sabin et al, 1960) A single dose of Sabin's oral polio vaccine produces immunity to all three poliovirus serotypes in about 50% of recipients. Three doses of live-attenuated OPV produce protective antibody to all three poliovirus types in more than 95% of recipients. (Human trials of Sabin's vaccine began in 1957, and in 1958 it was selected, in competition with the live vaccines of Koprowski and other researchers, by the US National

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Institutes of Health. Licensed in 1962, it rapidly became the only polio vaccine used worldwide. (Pasteur, 2009)

OPV is inexpensive, easy to administer, and produces excellent immunity in the intestine (which helps prevent infection with wild virus in areas where it is endemic), and has therefore been the vaccine of choice for controlling poliomyelitis in many countries. On very rare occasions (about one case per 750,000 vaccine recipients), the attenuated virus in OPV reverts into a form that can paralyze. (Racaniello, 2006)

There are various types of the OPV which include the trivalent OPV (tOPV), Bivalent OPV (bOPV) and the monovalent OPV(mOPV).

2.6   Epidemiology of Poliomyelitis

While now rare in the Western world, polio is still endemic to South Asia and Africa, particularly Pakistan and Nigeria respectively. Following the widespread use of poliovirus vaccine in the mid-1950s, the incidence of poliomyelitis declined dramatically in many industrialized countries. A global effort to eradicate polio began in 1988, led by the World Health Organization, UNICEF, and The Rotary Foundation.   These efforts have reduced the number of annual diagnosed cases by 99%; from an estimated 350,000 cases in 1988 to a low of 483 cases in 2001, after which it has remained at a level of about 1,000 cases per year (1,606 in 2009).

In 2012, cases decreased to 223. (CDC, 2013) Polio is one of only two diseases currently the subject of a global eradication program, the other being Guinea worm disease. So far, the only diseases completely eradicated by humankind are smallpox, which happened in 1979, (WHO ,2008) and rinderpest in 2010. A number of eradication milestones have already been reached, and several regions of the world have been certified polio-free. The Americas were declared polio-free in 1994. (CDC, International Notes Certification of Poliomyelitis eradication- the Americas, 1994)

In 2000 polio was declared to have been officially eliminated in 37 Western Pacific countries, including China and Australia. Europe was declared polio-free in 2002. As of 2013, polio remains endemic in only three countries: Nigeria, Pakistan, and Afghanistan, although it

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continues to cause epidemics in other nearby countries due to hidden or reestablished transmission. For example, despite eradication ten years prior, an outbreak was confirmed in China in September 2011 involving a strain prevalent in neighboring Pakistan. Since January 2011, there have been no reported cases of the wild polio infections in India, and in February 2012 the country was taken off the WHO list of polio endemic countries. It is reported that if there are no cases of wild polio in the country for two more years, it will be declared as a polio-free country. (Ray, 2012)

2.7 Poliomyelitis in the Vaccinated

It is a known fact that poliomyelitis occurs in both vaccinated and unvaccinated children Despite vaccination many children still come down with Poliomyelitis and this is a phenomenon that is global occurring world wide .In 2012 for example 77% of the children who took many doses of OPV still came down with wild Poliovirus infection in Nigeria, (WHO,2012) Reports, mostly in the Indian literature, indicate an increasing proportion of acute paralytic poliomyelitis among children who had been immunized with three doses of trivalent oral poliomyelitis vaccine (tOPV3, with 70-85% coverage), ranging from 10% to 26% among hospital studies (Sen et al, 1989), (Deivanayagam et al, 1991)

There was a report in the International News 2009 in Pakistan of a 10 month old fully vaccinated baby who had poliomyelitis after receiving all routine and additional doses of OPV during different campaigns right since birth.

There was also the case of Polio in an 18month old baby who had 3 polio vaccinations in Pakistan 2009.

The Dawn 2010 reported that 785 of polio cases in Pakistan were vaccinated people.

2.8 Description of the Clinical Effectiveness of Oral Polio Vaccine

Clinical Effectiveness can be described as the protective efficacy of vaccines in the field or community settings as against vaccine efficacy that is measured in ideal situations and control settings.

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Vaccine effectiveness is often confused with vaccine efficacy (in fact, one former designation for it was "field efficacy") but should be viewed as a distinctly different, although related, concept (Clemens et al, 1996)

Essentially, vaccine effectiveness is a " real world" view of how a vaccine (which may have already proven to have high vaccine efficacy) reduces disease in a population. This measure can assess the net balance of benefits and adverse effects of a vaccination program, not just the vaccine itself, under more natural field conditions rather than in a controlled clinical trial. Vaccine effectiveness is proportional to vaccine potency (ie, vaccine efficacy) but is also affected by how well target groups in the population are immunized (which itself may reflect difficulties in maintaining proper storage conditions of a vaccine, such as the cold chain, access to health care, and vaccine cost), as well as by other nonvaccine-related factors that influence the real-world outcomes of hospitalizations, ambulatory visits, or costs.

2.9   Scientific methods of measuring effectiveness of vaccines

Several study designs may be used to measure vaccine effectiveness (Orenstein et al, 1988)

Perhaps the most familiar is the retrospective case control analysis, in which the rates of vaccination among a set of infected cases and appropriate controls are compared (Clemens et al, 1996); (Orenstein et al, 1985). The outcome data (vaccine effectiveness) are expressed as a rate difference, with use of the odds ratio (OR) for developing infection despite vaccination:

$$VE = 1 - OR \times 100$$

A less well-known type of study design to measure vaccine effectiveness is the " indirect cohort" or " quasi-cohort" study, in which different responses in the same vaccinated population are examined (Clemens et al, 1996) For example, an analysis of the vaccine effectiveness of pneumococcal polysaccharide vaccine examined all invasive pneumococcal disease in a population cohort and compared the rates of vaccine-serotype infection and nonvaccine-serotype infection (assuming that no protection against nonvaccine serotypes was afforded by vaccination), providing an indirect estimate of vaccine effectiveness (Broome et al, 1980)

Another uncommon type of vaccine effectiveness study is the " case-coverage" or " case-cohort" method, in which vaccination rates among cases are compared with those in a similar cohort (which may include individuals who develop cases) over a defined period of time (Szilagyi et al, 2008)

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The fourth type of vaccine effectiveness study, used by Curns et al to assess the impact of rotavirus vaccine, is ecologic or observational in nature, examining changes in disease burden over time (eg, before and after introduction of routine vaccination) (Curns et al, 2010)

The " real world" view afforded by vaccine effectiveness data is desirable in planning public health initiatives, an advantage (along with a simpler and less costly study design) that makes these studies attractive. (Orenstein et al, 1988)

2.10   Factors affecting vaccine effectiveness

Many biases (some of which are difficult to detect) can affect vaccine effectiveness studies, such as differential case ascertainment in vaccinated and unvaccinated groups, differences in susceptibility or exposure of some groups in the population to infection, differences in health care utilization (unrelated to vaccination) between vaccinated and unvaccinated populations, undetected loss to follow-up from migration, and assumptions made during statistical analysis. Thus, vaccine effectiveness studies have the benefit of using real-world outcomes but also possess challenges in distinguishing vaccine-related effects from other potential confounders that may affect the same outcomes. (Clemens et al, 1996)

In a study carried out in Madras city, as the number of doses increased from 1 to 3, there was a trend for increase in VE for both the 6-35 and 6-23 months age groups .

An unimmunized child was at 5 times greater risk of developing paralysis than fully immunized Children, those who received 1 and 2 doses were at 4.2 and 2.8 times greater risk, respectively.

The observation was similar to the estimated field efficacy of 90% in Bombay city based on the data from coverage surveys of children aged 12-23 months and immunization status of cases (Farley, 1989)

Also, in another study, the VE by case-control study for two countries in Taiwan for three or more TOPV doses in children aged 12 to 35 months was estimated to be 96% .

A recent report of a case-control study in Delhi, using neighbourhood controls, has estimated VE to be 92% (singh et al, 1992)

A case-control study was carried out between May 1988 and May 1989 to assess the effectiveness of three doses of trivalent oral poliomyelitis vaccine (tOPV3) in children aged 6-35 months in Madras city. Reports show that all the cases were patients with acute paralytic

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poliomyelitis who were residing in Madras city and were hospitalized in the Institute of Child Health; they represented 95% of such cases in the city. The <u>diagnosis</u> was based on <u>clinical</u> grounds and confirmed by stool culture which was positive in 60%. Age- and sex-matched controls, all residing in the city of Madras, were recruited concurrently from the Institute's outpatient department. There were 78 cases and 315 controls. Vaccine efficacy observed for TOPV3 was 81% (95% CI, 58-91%) for the 6-35-month age group and 86% (95% CI, 67-94%) for the 6-23-month age group. Vaccine efficacy, after controlling for age using the Mantel-Haenszel method, was 83% (95% CI, 67-91%). An <u>unimmunized</u> child was at 5 times greater risk of developing acute paralytic poliomyelitis than a fully <u>immunized</u> child (Deivanayagam et al, 1991)

2.11   Receiver Operating Characteristic Curve

In signal detection theory, a receiver operating characteristic (ROC), or simply ROC curve, is a graphical plot which illustrates the performance of a binary classifier system as its discrimination threshold is varied. It is created by plotting the fraction of true positives out of the total actual positives (TPR = true positive rate) vs. the fraction of false positives out of the total actual negatives (FPR = false positive rate), at various threshold settings. TPR is also known as sensitivity or recall in machine learning. The FPR is also known as the fall-out and can be calculated as one minus the more well known specificity. The ROC curve is then the sensitivity as a function of fall-out. In general, if both of the probability distributions for detection and false alarm are known, the ROC curve can be generated by plotting the Cumulative Distribution Function (area under the probability distribution from -inf to +inf) of the detection probability in the y-axis versus the Cumulative Distribution Function of the false alarm probability in x-axis.

ROC analysis provides tools to select possibly optimal models and to discard suboptimal ones independently from (and prior to specifying) the cost context or the class distribution. ROC analysis is related in a direct and natural way to cost/benefit analysis of diagnostic decision making.

The ROC curve was first developed by electrical engineers and radar engineers during World War II for detecting enemy objects in battlefields and was soon introduced to psychology to account for perceptual detection of stimuli. ROC analysis since then has been used in medicine,

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radiology, biometrics, and other areas for many decades and is increasingly used in machine learning and data mining research. The ROC is also known as a relative operating characteristic curve, because it is a comparison of two operating characteristics (TPR and FPR) as the criterion changes. (Swets et al, 1996)

The receiver operating characteristic (ROC) curve is the plot that displays the full picture of trade-off between the sensitivity (true positive rate) and (1- specificity) (false positive rate) across a series of cut-off points. Area under the ROC curve is considered as an effective measure of inherent validity of a diagnostic test. This curve is useful in (i) evaluating the discriminatory ability of a test to correctly pick up diseased and non-diseased subjects; (ii) finding optimal cut-off point to least misclassify diseased and non-diseased subjects; (iii) comparing efficacy of two or more medical tests for assessing the same disease; and (iv) comparing two or more observers measuring the same test (inter-observer variability).

2.12   Methods to find the 'optimal' threshold point

Three criteria are used to find optimal threshold point from ROC curve. First two methods give equal weight to sensitivity and specificity and impose no ethical, cost, and no prevalence constraints. The third criterion considers cost which mainly includes financial cost for correct and false diagnosis, cost of discomfort to person caused by treatment, and cost of further investigation when needed. (Curns et al, 2010)

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CHAPTER THREE

METHODOLOGY

3.1   Study Area

The study was carried out in Nigeria. Nigeria is the most populous country in Africa, with a population of 148 million in 2007 and a growth rate of 3.8% per annum. The estimated life expectancy is on average 48 years, with an infant mortality rate of 99 per 1000. Nigeria has six regional zones that reflect varying ecologies, climates and population characteristics. The zones are divided into 36 States and the Federal Capital Territory, which are further divided into 774 LGAs and 8812 administrative wards.

3.2   Study Population

Children with reported Acute Flaccid Paralysis between 0 and 15 years of age in the 36 states of the Federation of Nigeria including FCT between 2009 and 2012 were included in this study.

3.3   Study Design and Duration

This study was carried out using a Secondary data Analysis of the National Polio Surveillance System data consisting of all the 36 states of the Federation and the Federal Capital Territory between 2009 and 2012.The Study Design used is a Retrospective review of the secondary data which was obtained from the national AFP Surveillance data of the World Health Organization. 3.4 The original data was obtained in the MS Excel data base format and this was converted to SPSS Version 15.The data is gotten from the AFP Surveillance of the country.

Preliminary cleaning was done on the data which included extraction of relevant information from other related variables that can be analyzed. Example 'the age in months' that was gotten from date of birth.'

Frequency distribution were run to explore the distribution of the various variables and categories were summarized into functional groups.

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3.4   Description of the surveillance system

Surveillance for poliomyelitis relies on the reporting of children under 15 years old with AFP through a network of health providers. These children undergo a clinical and epidemiological assessment, including the collection of two stool samples within 14 days of the onset of paralysis, which are tested for the presence of poliovirus. Most countries implementing AFP surveillance currently meet the WHO target of at least one case of AFP reported each year per 100 000 children under 15 years old, although there can be significant variability at the subnational level. Currently more than 100 000 children with AFP are investigated each year, giving polio eradication one of the most comprehensive and sensitive surveillance networks in global public health.

Data collection started at various Health Facilities including maternity centres in various Local Government Areas of the States of the Federation with the use of (CIFs): Case Investigation Forms. Health workers who detect suspected cases notify the Disease surveillance notification workers who investigate the cases. The Health workers look for cases in which children less than 15 years who were once walking suddenly lose the ability to walk and their legs or one of their legs become floppy with muscle weakness occurring within two months of report or detection. Sudden loss of muscle tone in the legs can also be an indication of paralysis in younger children not yet walking. This may or may not be accompanied with fever.

The Disease surveillance Notification Officers (DSNOs) collected two stool samples at least 24 hours apart from theses children (0 to 15 years) that presented with AFP (Acute Flaccid Paralysis) from all these LGAs in all the states of the Federation. The AFP stool samples collected in appropriate containers and are stored at appropriate temperature in freezers and then taken to the WHO National Polio Laboratory using ice packs placed in giostyles with the aim of maintaining the reverse cold chain.

There are two laboratories that receive these stool samples namely the WHO National Polio Laboratory Ibadan which handles 26 States & FCT and the WHO National Polio Laboratory Maiduguri which handles 10 States (mainly in the North). The two samples collected 24 to 48 hours apart are received by the Laboratories and stored appropriately and the condition on receipt noted. A Good sample is one in which the reverse cold chain is maintained (2-8 degrees

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Centigrade), is of adequate quantity, has no desiccation and no leakage. The information is also recorded in the Laboratory registers and entered into the Laboratory database accordingly.

The Samples collected are processed in the Laboratory using glass beads ,Phosphate Buffered Solution containing magnesium and calcium ions for stabilizing the virus) & Chloroform (to remove all pyrogens, lipids and unwanted bacteria.),Centrifuged at1500Rpm and inoculated into L20B(a genetically engineered mouse cell line) and RD (Rhabdomyosarcoma) Cell lines. The Cell lines are observed for Cytopathic Effect (CPE) for 10 days (Primary and Secondary(Blind) passage). Poliovirus isolates that are obtained are then sent to the Intratypic differentiation unit for further characterization. Intratypic Differentiation (ITD) is performed on Isolates using Real Time Polymerase Chain Reaction (PCR) (ITD and VDPV PCR) to determine whether they are wild or sabin Polio virus. Enzyme linked immune sorbent assay, Conventional PCR and Probe Hybridization tests can also be carried out. The results obtained are then sent to the Data management unit for entering of the results into the database. The Data of the result is entered as Wild or Sabin Polio, Vaccine derived poliovirus (VDPV), Non Polio or Negative, cleaned and data harmonization done quarterly.

Data Management and analysis was done using EPI INFO designed by CDC (Centre for Disease Control) and Results are forwarded and reported for programmatic action. Finally, variables present in the data set include state, age in months, sex and total Polio doses

3.5   Data Extraction, Analysis and Interpretation:

This was done with the use of SPSS (Statistical Package for Social Science) Version 15 - Descriptive statistics and bivariate Analysis ;(Chi Square test) were carried out. A review of 2009-2012 cases with a sample size of approximately 5000 AFP cases per year was carried out. Relevant data was extracted from available variables and analyzed. Descriptive statistics including frequency tables and bar charts were used for the determination of the Pattern of AFP cases and Wild Polio virus. ODDs Ratio was used for the determination of the clinical effectiveness of the Oral Polio vaccine. Logistic Regression was done to exclude other factors related to the occurrence of Wild Polio Virus our outcome variable. Receiver Operating Characteristic Curve was used to determine optimum OPV dose by determining values of best Sensitivity and Specificity.

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3.6   Data collection Instrument

The Case Definition of AFP used is "Any *case of AFP in a child aged <15 years, or any case of paralytic illness in a person of any age when polio is suspected.*" The Instrument used for collection of the data is the Case Investigation Form (CIF) which is available in 4copies. The information obtained is manually written on the form.

Such information include name of the patient, name of the parents, home address, date of birth, OPV vaccination history (Number of OPV doses taken), Date of onset of paralysis, date of last OPV dose, type of paralysis. The DSNO will assign an Epidemiological Number (Epid. NO) to the case and will also record details of date 1st and 2nd stool collected, date sent to the lab and other details.

3.7   Ethical Consideration

The Confidentiality of the AFP case- patients was protected by the use of de-identified and coded data and permission was obtained from the World Health Organization Nigeria.

CHAPTER FOUR

RESULTS

4.1   Socio-demographic and other Characteristics of AFP cases and Wild Poliovirus

A total of 24848 Acute Flaccid Paralysis (AFP) cases were involved in the study with a mean age of 36months (SD=±33months), median of 28 months and range 252 months. The highest proportion of children with AFP was among the 12-23 months age group representing a quarter of the total cases while the lowest proportion was among those in the 48-59 months age group. Gender distribution was males (57%) and females (43%). AFP samples were more than a quarter (29%) in the North-West zone of the country indicating the zone with the highest proportion, followed by similar proportions of 16% each in the other two zones from the north. Moreover, AFP cases were found to be least in the South-East and South-West zones with a proportion of 11%. There was an increase in the proportion of AFP cases as the years progressed from 22% in 2009 to 29% in 2012. Of the total Acute Flaccid Paralysis cases in the data base, 3.6% of them had zero OPV dose, 11.2% had between 1-2 doses, and 14.6% had 3 doses while more than two-third had greater than 3 doses. All these are shown in table 4.1
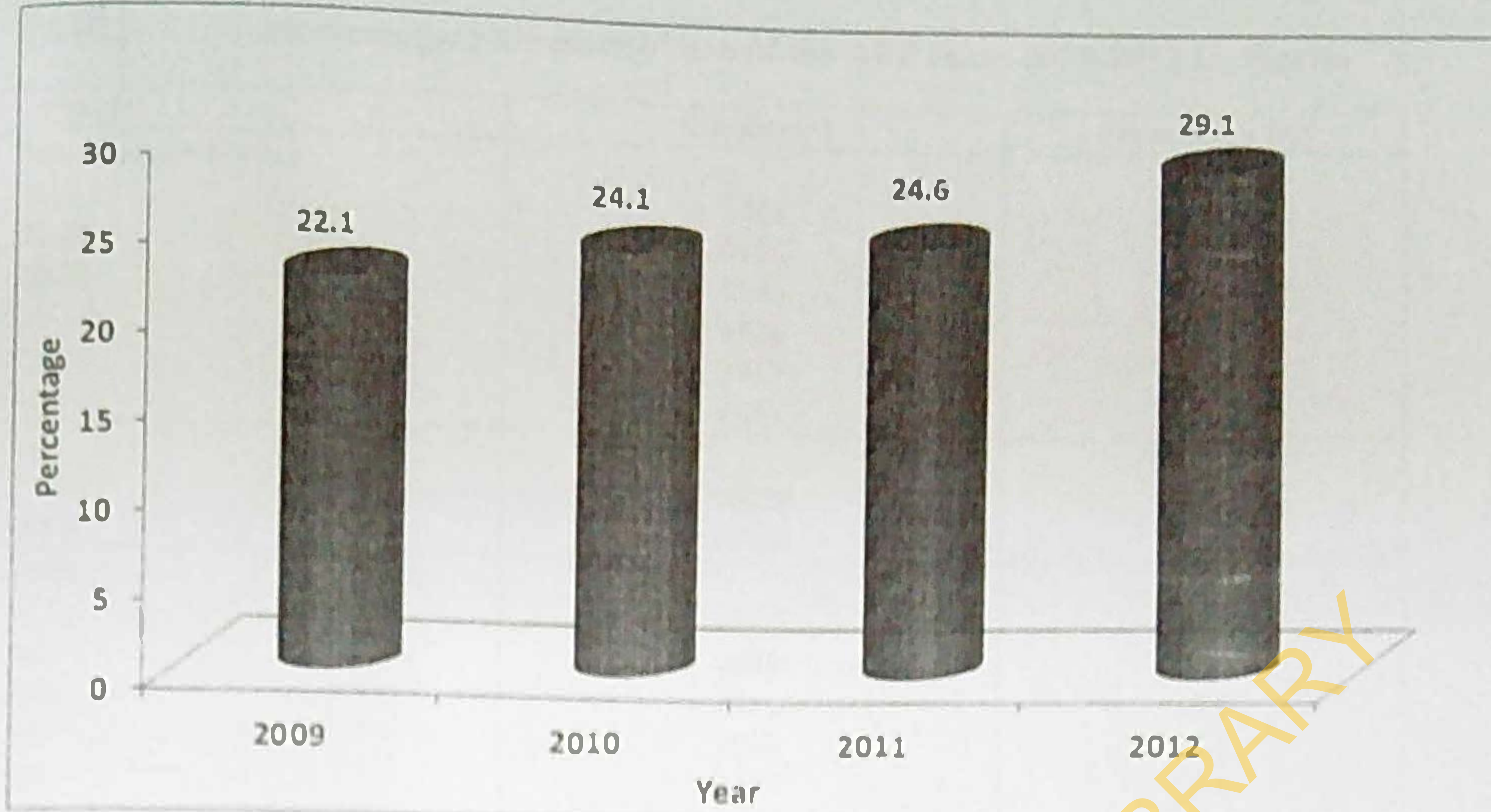
FIGURE 4.1: Percentage distribution of AFP cases by year (2009-2012) in Nigeria

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TABLE 4.1: Socio-demographic distribution of the AFP cases 2009-2012 in Nigeria

Variables	Number(n)	Percentage (%)
Age-group(months)		
<12	2743	11.0
12-23	6114	24.6
24-35	5545	22.3
36-47	3579	14.4
48-59	2267	9.1
60+	4591	18.5
Sex		
Female	10689	43.0
Male	14154	57.0
Zone		
NC	4140	16.7
NE	4085	16.4
NW	7215	29.0
SE	2755	11.1
SS	3687	14.8
SW	2966	11.9
Year		
2009	5501	22.1
2010	6000	24.1
2011	6108	24.6
2012	7239	29.1
OPV doses		
0	899	3.6
1-2	2781	11.2
3	3612	14.6
>3	17555	70.7
Total	**24848**	**100.0**

Note:

NC: North Central

NE: North East

NW: North West

SE: South East

SS: South South

SW: South West

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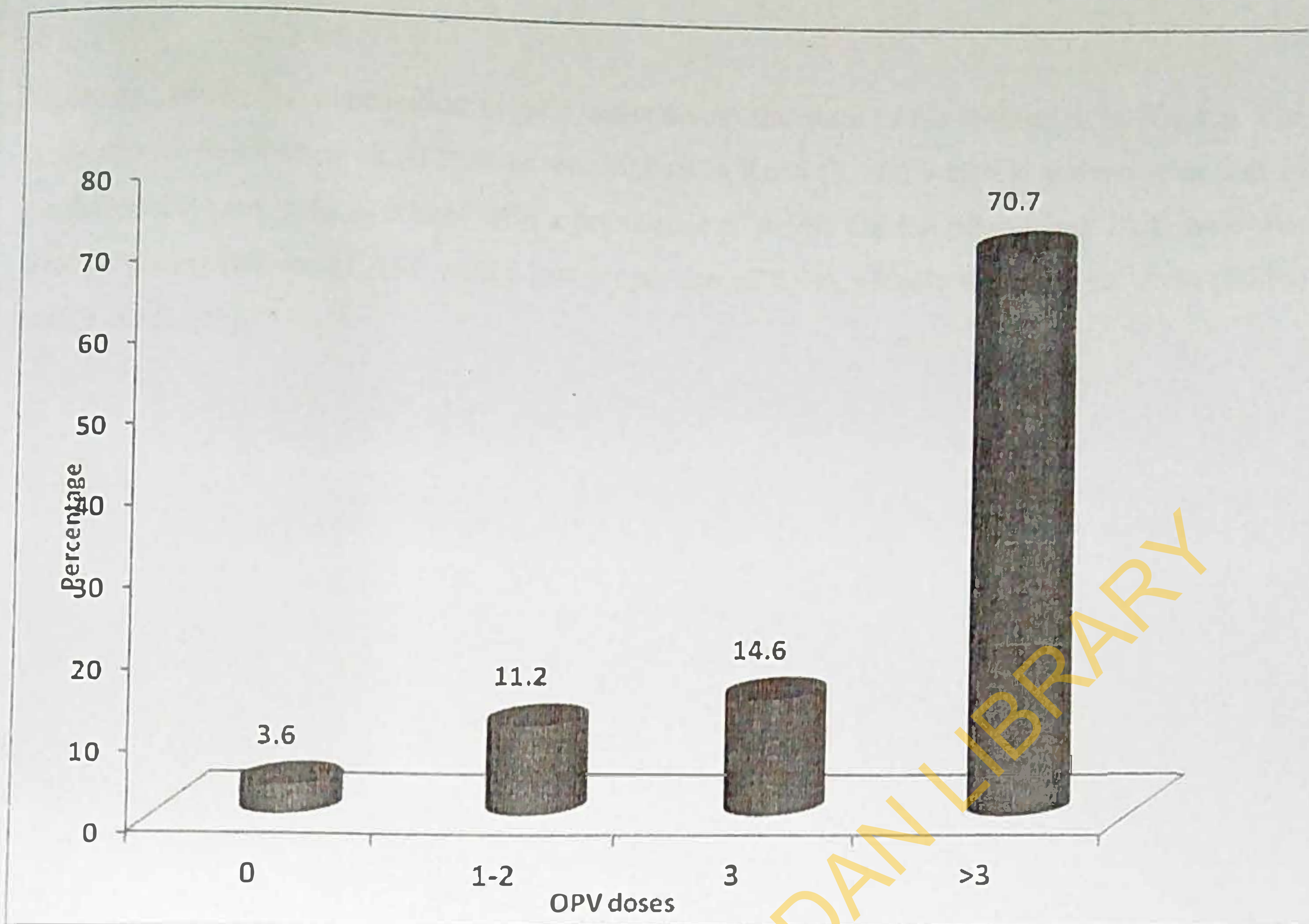
FIGURE 4.2 : Chart showing the Distribution of total OPV doses among AFP cases 2009-2012 in Nigeria

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Figure 4.3 shows the distribution of AFP cases across the state of the federation in Nigeria. The proportional distribution of AFP cases was highest in Kano (8.1%) which is almost twice that of the following next state of Kebbi with a prevalence of 4.5%. On the other hand, Ekiti state was least in the prevalence of AFP with a low proportion of 0.9%, closely followed by Ondo (1.2%) and Osun (1.4%).

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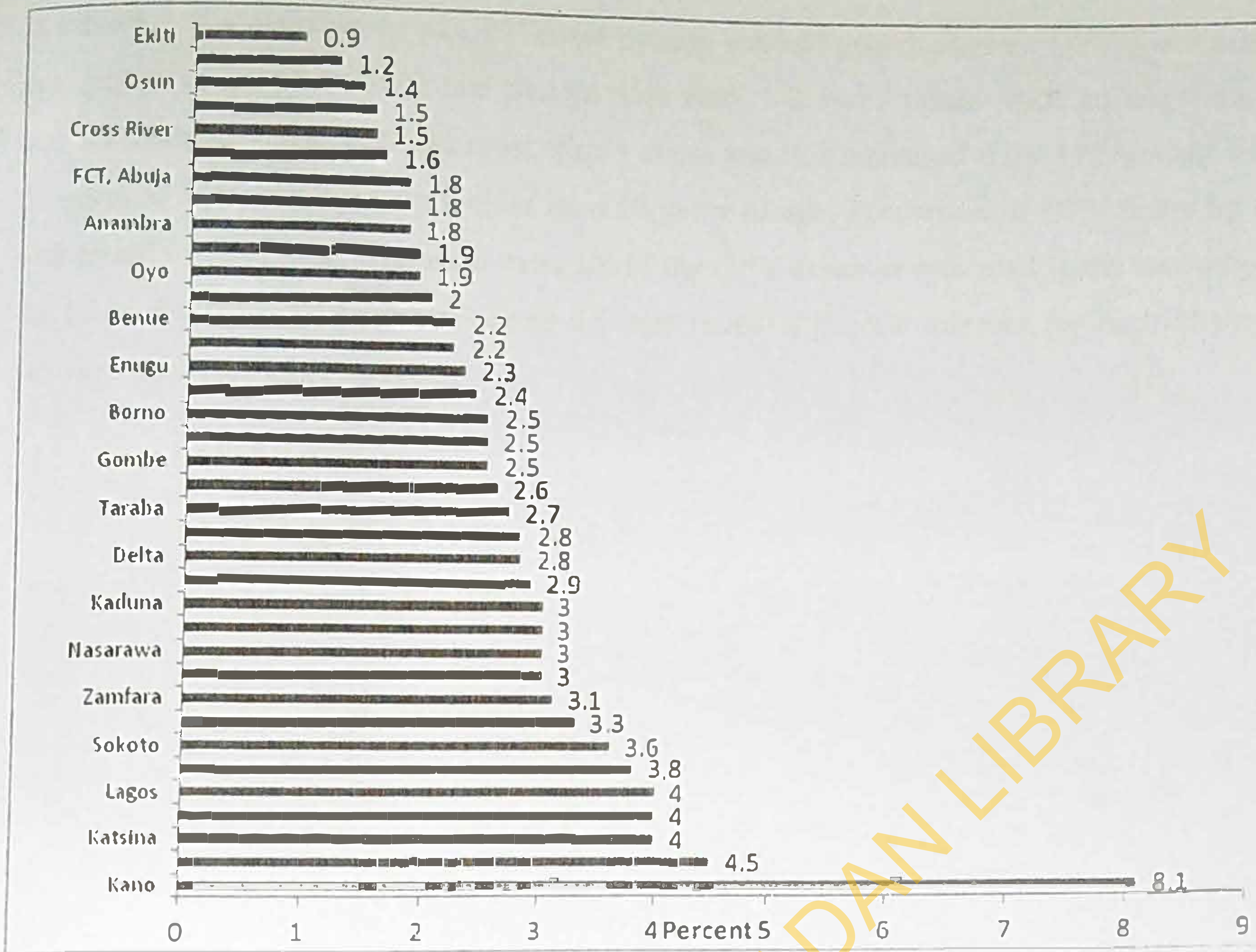
FIGURE 4.3: Chart showing the Distribution of AFP cases by state in Nigeria 2009-2012

In table 4.2, the distribution of OPV doses by age, sex and year is shown. OPV doses across the age groups revealed no particular pattern with zero, 1-2 and 3 doses while an increasing trend was seen among those who had more than 3 doses and this increased from 45% among less than 12 years to 78% among people older than 60 years of age. Proportion of OPV doses by gender was found to be similar with each category of the OPV doses as indicated in the second pane of the table. However, OPV doses across the year reveal a general increase for each of the doses between the years 2009 to 2012.

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TABLE 4.2: Distribution of Age, Sex and year by OPV doses

Variable	Doses				Total
	0 dose	1-2 doses	3 doses	>3 doses	
Age group					
<12	134(4.9)	736(26.8)	650(23.7)	1223(44.6)	2743
12-23	206(3.4)	640(10.5)	978(16.0)	4289(70.2)	6114
24-35	209(3.8)	584(10.5)	762(13.7)	3990(72.0)	5545
36-47	91(2.5)	337(9.4)	420(11.7)	2731(76.3)	3579
48-59	72(3.2)	182(8.0)	264(11.6)	1749(77.2)	2267
60+	187(4.1)	302(6.6)	537(11.7)	3565(77.7)	4591
Sex					
Female	375(3.5)	1195(11.2)	1567(14.7)	7551(70.6)	10689
Male	524(3.7)	1585(11.2)	2044(14.4)	10001(70.7)	14154
Year					
2009	319(5.8)	932(16.9)	1016(18.5)	3234(58.8)	5501
2010	213(3.6)	659(11.0)	1042(17.4)	4085(68.1)	6000
2011	191(3.1)	551(9.0)	767(12.6)	4599(75.3)	6108
2012	176(2.4)	639(8.8)	787(10.9)	5637(77.9)	7239
Total	899(3.6)	2781(11.2)	3612(14.5)	17555(70.7)	24848

The distribution of OPV doses and zone is shown in table 4.3. The North Western zone had the highest proportion (7.1%) of children who had received no OPV doses. Interestingly, the North Central zone the highest proportion (85.2%) of children who had received the highest number of oral polio vaccine doses and also the lowest percentage with 0 doses. In a similar vein, the South West, North-East and South-South zones had children who had received at least 4 doses of OPV representing more than 70% of the children.

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Table 4.3: Distribution of Oral Polio vaccine doses by zone in Nigeria 2009-2012

Zone	Doses				Total
	0 dose	1-2 doses	3 doses	>3 doses	
NC	59(1.4)	230(5.6)	324(7.8)	3527(85.2)	4140
NE	127(3.1)	436(10.7)	527(12.9)	2995(73.3)	4085
NW	511(7.1)	1118(15.5)	1075(14.9)	4510(62.5)	7215
SE	88(3.2)	361(13.1)	646(23.4)	1660(60.3)	2755
SS	61(1.7)	381(10.3)	656(17.8)	2589(70.2)	3687
SW	53(1.8)	255(8.6)	384(12.9)	2274(76.7)	2966
Total	899(3.6)	2781(11.2)	3612(14.5)	17555(70.7)	24848

The highest proportion of wild Poliovirus (3.5%) was seen among children aged 24-35months and the least among children older than 60months (1%). Proportion of present wild Poliovirus between gender was the same (2.3%). However, wild Poliovirus presence was highest in the year 2009 (7.1%) and decrease thereafter to 0.4% which was least in the year 2010 while a decrease compared to year 2009 was also observed in year 2011 and 2012. Across the zone, AFP cases with wild poliovirus was high in the Northern zones with the highest seen in the North central (5.3%). The highest proportion (12.9%) of AFP cases with Wild Polio was among children with zero doses of Oral Polio virus and lowest (1.2%) among children who had more than 4 OPV doses. An increase was also noticed in the occurrence of Wild poliomyelitis as the number of OPV doses taken reduces.

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Table 4.4: Distribution of Socio-demographic factors by wild Poliovirus among AFP cases between 2009 and 2012 in Nigeria

Variable	Wild Poliovirus		Total	P Value
	Present	Absent		
Age group				
<12	42 (1.5)	2701 (98.5)	2743	
12-23	165 (2.7)	5949 (97.3)	6114	
24-35	196 (3.5)	5349 (96.5)	5545	0.00006
36-47	89 (2.5)	3490 (97.5)	3579	
48-59	55 (2.4)	2212 (97.6)	2267	
60+	46 (1.0)	4545 (99.0)	4591	
Sex				
Female	247 (2.3)	10442 (97.7)	10689	0.521
Male	346 (2.4)	13808 (97.6)	14154	
Year				
2009	388 (7.1)	5113 (92.9)	5501	
2010	21 (0.4)	5979 (99.7)	6000	0.0000
2011	63 (1.0)	6045 (99.0)	6108	
2012	121 (1.7)	7118 (98.3)	7239	
Zone				
NC	50 (1.2)	4090 (98.8)	4140	
NE	125 (3.1)	3960 (96.9)	4085	
NW	382 (5.3)	6833 (94.7)	7215	0.0000
SE	3 (0.1)	2752 (99.9)	2755	
SS	13 (0.4)	3674 (99.6)	3687	
SW	20 (0.7)	2946 (99.3)	2966	
OPV doses				
0	116(12.9)	783(87.1)	899	
1-2	167(6.0)	2614(94.0)	2781	0.0000
3	102(2.8)	3510(97.2)	3612	
>3	208(1.2)	17347(98.8)	17555	
Total	**593(2.0)**	**24254(98.0)**	**24848**	

In table 4.5, the proportion of children with Wild Polio Type 3 (61%) was higher than children with Wild Polio type 1 (39%). Among the various age groups, the proportion of children (46%) with WPV1 was highest in the age group 12-23month while the proportion of children (67%) with WPV3 was highest in the age group 48-59month. WPV1 and WPV3 were found to be similar in both sexes of children .Across the year, the proportion of WPV1 was found to increase from 19.3% in 2009 to 84.3% in 2012 while on the other hand, the proportion of WPV3 was found to decrease from 80.7% in 2009 to 15.7% in 2012. WPV1 was also more predominant in the Southern part of Nigeria and WPV3 was prevalent in the Northern zones. Although WPV1 was highest among children aged 12-23 months it was more common among younger children. WPV3 was similar (at least 60%) across the age groups except in age group 12-23 months.

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TABLE 4.5: Distribution of socio-demographic characteristics by wild type

Variable	Wild Type		Total
	Type 1	Type 3	
Age group			
<12	16(38.1)	26(61.9)	42
12-23	76(46.1)	89(53.9)	165
24-35	73(37.2)	123(62.8)	196
36-47	33(37.1)	56(62.9)	89
48-59	18(32.7)	37(67.3)	55
60+	16(34.8)	30(65.2)	46
Sex			
Female	97(39.3)	150(60.7)	247
Male	135(39.0)	211(61.0)	346
Year			
2009	75(19.3)	313(80.7)	388
2010	8(38.1)	13(61.9)	21
2011	47(74.6)	16(25.4)	63
2012	102(84.3)	19(15.7)	121
Zone			
NC	29(58.0)	21(42.0)	50
NE	22(17.6)	103(82.4)	125
NW	146(38.2)	236(61.8)	382
SE	3(100.0)	0(0.0)	3
SS	12(92.3)	1(7.7)	13
SW	20(100.0)	0(0.0)	20
OPV doses			
0	55(47.4)	61(52.6)	116
1-2	59(35.3)	108(64.7)	167
3	29(28.4)	73(71.6)	102
>3	89(42.8)	119(57.2)	208
Total	232(39.1)	361(60.9)	593

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4.2 Clinical Effectiveness of the OPV

Table 4.6 shows the clinical effectiveness of OPV between the two age-group stratifications and location. Vaccine efficacy among the younger children for 1-2 doses was 70% and this proportion increases with increasing number of OPV doses to 93% at 4 or more doses. However, among the older children, vaccine efficacy was rather low (5%) at the initial 1-2 doses but went up substantially thereafter to 65% at 3 doses and 89% at 4 or more doses. Clinical effectiveness of Oral Polio vaccine was higher in Northern Nigeria compared to the South. Vaccine effectiveness in Southern Nigeria was twice that of Northern Nigeria at 1-2 OPV doses. Overall, vaccine effectiveness was found to increase with the number of doses.

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TABLE 4.6: Clinical effectiveness of OPV

Variables	Odds Ratio(95% C.I)	Vaccine effectiveness (%)
Less than 35months		
1-2	0.30(0.22, 0.40)	70.0
0(ref)	1.0	
3	0.15(0.11, 0.21)	85.0
0(ref)	1.0	
>3	0.07(0.06, 0.10)	93.0
0(ref)	1.0	
Greater than 35months		
1-2	0.95(0.59, 1.53)	5.0
0(ref)	1.0	
3	0.35(0.20, 0.59)	65.0
0(ref)	1.0	
>3	0.11(0.07, 0.18)	89.0
0(ref)		
All age-group		
1-2	0.43(0.34, 0.55)	57.0
0(ref)	1.0	
3	0.20(0.15, 0.26)	80.0
0(ref)	1.0	
>3	0.08(0.06, 0.103)	92.0
0(ref)	1.0	
Northern Nigeria		
1-2	0.55	45.0
0(ref)	1.0	
3	0.29	71.0
0(ref)	1.0	
>3	0.10	90.0
0(ref)	1.0	
Southern Nigeria		
1-2	0.12	88.0
0(ref)	1.0	
3	0.08	92.0
0(ref)	1.0	
>3	0.04	96.0
0(ref)	1.0	

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4.3 Association between Socio-demographic factors, OPV and occurrence of Wild Poliovirus

There was a statistically significant association between age-group, OPV dose, location and the presence of wild status of poliomyelitis. Younger children age <35months (2.8%) had a significantly higher proportion of wild Poliovirus compared to older children > 35months of age(1.8%). Higher proportion of wild poliomyelitis was similarly found among cases with zero OPV doses (12.9%) than cases who had at least 1 dose of OPV (2.0%) among the AFP cases. More also, the proportion of Northern children with the presence of wild poliomyelitis was about nine times the southern children (3.6% vs. 0.4%). However, no statistical association was detected between gender and the presence of wild poliomyelitis (P>0.05) as shown in table 4. 8.

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Table 4.7: Association of Socio demographic and occurrence of poliomyelitis

Variable	Wild status		Total	χ2-value,P-value
	Present	Absent		
Age group(months)				
<35	403(2.8)	14008(97.2)	14411	24.753, 0.000
>35	190(1.8)	10247(98.2)	10437	
Sex				
Female	247 (2.3)	10442 (97.7)	10689	0.468, 0.494
Male	346 (2.4)	13808 (97.6)	14159	
OPV status				
0 dose	116(12.9)	783(87.1)	1001	442.82, 0.000
1 dose plus	477(2.0)	23471(98.0)	23847	
Location				
Northern Nigeria	557(3.6)	14883(96.4)	15440	260.98, 0.000
Southern Nigeria	36(0.4)	9372(99.6)	9408	

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Table 4.7: Association of Socio demographic and occurrence of poliomyelitis

Variable	Wild status		Total	χ2-value,P-value
	Present	Absent		
Age group(months)				
<35	403(2.8)	14008(97.2)	14411	24.753, 0.000
>35	190(1.8)	10247(98.2)	10437	
Sex				
Female	247 (2.3)	10442 (97.7)	10689	0.468, 0.494
Male	346 (2.4)	13808 (97.6)	14159	
OPV status				
0 dose	116(12.9)	783(87.1)	1001	442.82, 0.000
1 dose plus	477(2.0)	23471(98.0)	23847	
Location				
Northern Nigeria	557(3.6)	14883(96.4)	15440	260.98, 0.000
Southern Nigeria	36(0.4)	9372(99.6)	9408	

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4.4   Socio-demographic and other predictors of the occurrence of Wild Poliovirus

Table 4.8 shows the socio-demographic predictors of the occurrence of Wild Poliovirus. Younger children (<35months) are about 2 times more likely to have Wild Polio virus than older children of greater than 35months of age and this was statistically significant in the multiple regression (P<0.0001). Moreover, children who had never received Oral Polio vaccination (0 doses of OPV) were found to be about 6 times more likely to have wild Poliovirus than those who had received one or more dose of OPV. This association was found to be statistically significant (P<0.0001). In the same vein, children who resides in the Northern part of Nigeria were found to be about 10 times more likely to have Wild poliovirus than those who reside in the Southern part of Nigeria and this also was found to be statistically significant (P<0.0001).

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Table 4.8: Socio-demographic predictors of occurrence of Wild Poliovirus

Variable	Odds Ratio	95% CI	P-value
Age-group(months)			
<35	1.717	1.439-2.049	<0.001
>35(Reference)	1.000		
OPV Dose			
0 dose	5.995	4.816-7.463	<0.001
1 dose Plus(Reference)	1.000		
Location			
Northern Nigeria	9.414	6.706-13.216	<0.001
Southern Nigeria(Ref)	1.000		

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Table 4.8: Socio-demographic predictors of occurrence of Wild Poliovirus

Variable	Odds Ratio	95% CI	P-value
Age-group(months)			
<35	1.717	1.439-2.049	<0.001
>35(Reference)	1.000		
OPV Dose			
0 dose	5.995	4.816-7.463	<0.001
1 dose Plus(Reference)	1.000		
Location			
Northern Nigeria	9.414	6.706-13.216	<0.001
Southern Nigeria(Ref)	1.000		

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4.5   Prediction of Optimum OPV dose

The best cut off points for prevention of occurrence of wild Poliovirus by the OPV doses that maximizes sensitivity and optimizes specificity is outlined in table 10 below. A cut-off point of 4 doses from this result may be chosen as optimal. At this level, the OPV displayed a sensitivity of 65% and specificity of 71%.

Table 4.9: Cut-off points values of OPV doses.

Dose of OPV	Sensitivity (%)	Specificity (%)
1	19.7	96.7
2	33.1	28.0
3	48.0	85.9
4	65.4	71.3
5	76.2	53.4
6	85.6	37.5
7	90.0	27.6
8	93.7	21.3
9	96.4	14.6
10	96.4	11.9

ROC Curve
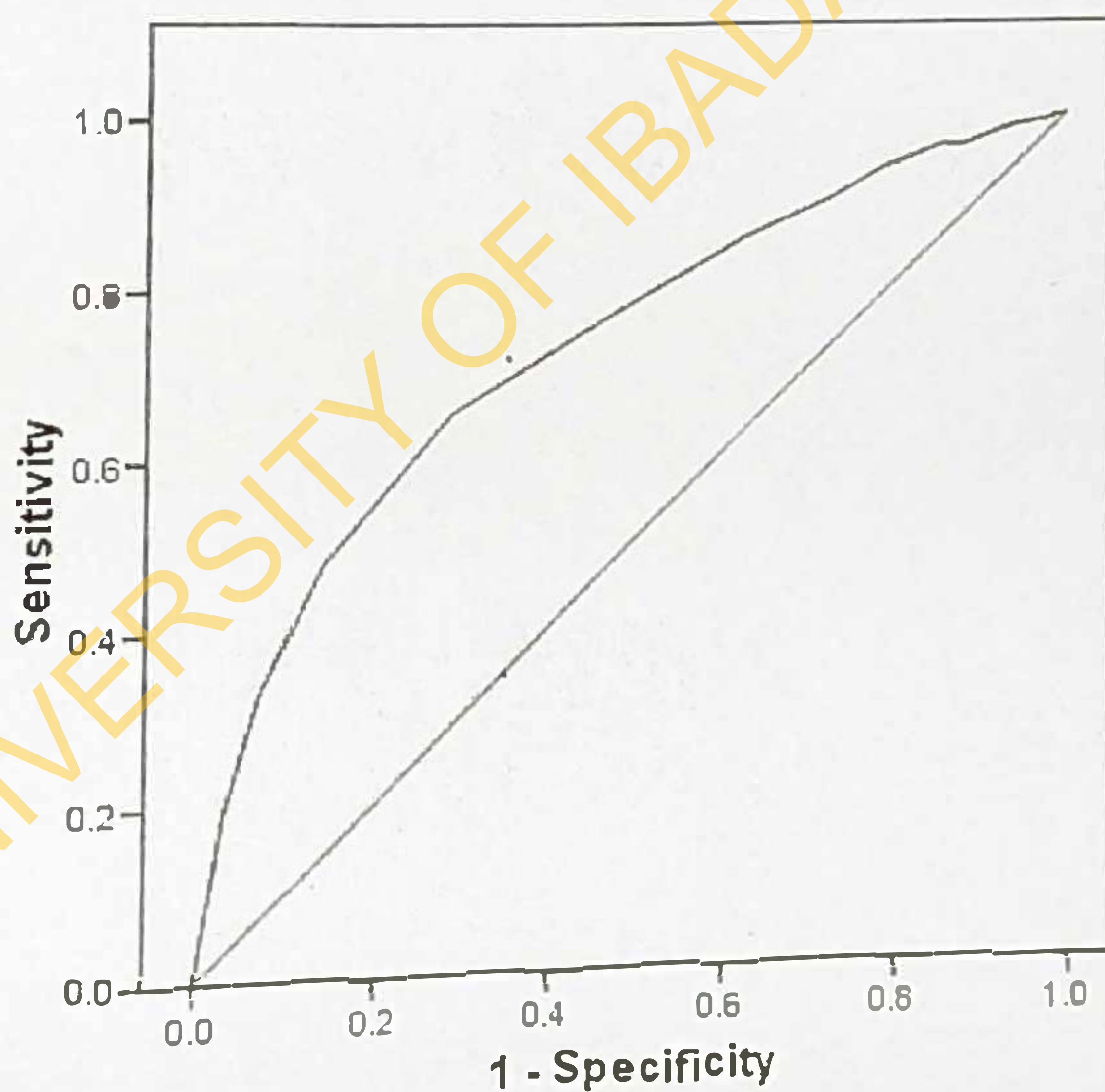
Figure 4.4: The ROC curve showing Sensitivity and Specificity at OPV doses1-10

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4.6 The Area under the ROC Curve

The Area under the ROC curve was 0.731 when the sensitivity and 1- Specificity of the OPV was plotted. This is very high showing that our findings are consistent in about 73% of cases.

TABLE 4.10: Area under the Receiver Operating Characteristic (ROC) Curve

	Area	P value	95% CI
Area under the Curve	0.731	0.000	0.709-0.753

CHAPTER FIVE

DISCUSSION

Poliomyelitis is endemic in Nigeria despite the fact that Oral Polio vaccine is routinely given to children and during other supplementary immunization activities. Four doses are given routinely at birth, 6, 10 and 14 weeks of age. The continued transmission of Wild Poliovirus in Nigeria is a serious threat to the eradication of Poliomyelitis globally as viruses from Nigeria can be imported and continue to cause epidemics in other nearby Countries due to hidden or reestablished transmission. (WHA, 2012). The eradication of Poliomyelitis has been declared as an emergency by the World Health Organization in 2014. With four doses being given routinely and yet the continued spread of the Poliovirus, it is possible that four doses are not sufficient for the prevention of the disease in Nigeria. There is therefore the need to determine the optimum dose required for prevention of the occurrence of Poliomyelitis in Nigeria.

Other Socio-demographic factors may also be associated with the continued occurrence of the disease and there is the possibility of reduced clinical effectiveness of the OPV under field condition in the actual community. This study focuses on the Epidemiology of AFP and Wild Poliovirus, determination of the Clinical effectiveness of the OPV and prediction of the optimum dose that will be protective against its occurrence.

5.1   Epidemiology of AFP cases

The review shows that in the distribution of AFP cases across the states of the federation in Nigeria, the occurrence of AFP cases was highest in Kano (8.1%) which is almost twice that of the following next state of Kebbi with a proportion of 4.5%. On the other hand, Ekiti state was least in the incidence of AFP with a low proportion of 0.9%, closely followed by Ondo (1.2%) and Osun (1.4%). This shows a higher proportion of AFP cases in the Northern part of Nigeria compared to the South indicating high level of transmission of Poliovirus in the North. This is consistent with previous studies which revealed that the distribution of Poliovirus isolates in relation to location showed highest number of the Poliovirus isolates in Zamfara State, followed by Kaduna, Niger, and Sokoto States (Northern states) while the least were found in Abia and Delta States (Southern states) (Adedeji et al, 2012)

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The Poliovirus isolates used by Adedeji et al in 2012 was a combination of only Sabin and Wild viruses while the AFP cases used in this study included Negatives, Non Polio Enteroviruses, Sabins and Wild Poliovirus. It is therefore interesting to note the similarities observed in these studies despite the differences between AFP cases and Poliovirus Isolates used in the studies.

The highest proportion of children with AFP was found among the 12-23 months age group representing a quarter of the total cases while the lowest proportion was among those in the 48-59 months of age(older age group) consistent with the findings of (Grassly et al, 2007) where the highest proportion of AFP cases was among age group 12-23 months. However, this is a deviation from the findings of Adedeji et al, 2012 in which most cases occurred between six months of age and four years.

Overall gender distribution of AFP cases (paralysis) was more of males (57%) than females (43%) and is consistent with findings by Adedeji ,et al 2012 which states that boys are more commonly paralysed. Of the total Acute Flaccid Paralysis cases in the data base, 3.6% of them had zero OPV dose, 11.2% had between 1-2 doses, and 14.6% had 2 doses while more than two-third had at least 4 doses.

This shows that only two thirds of children are adequately being vaccinated in Nigeria and explains the reason why Poliomyelitis is still endemic in our Nation. This shows poor immunization coverage in Nigeria.

5.2   Epidemiology of Wild Poliovirus

Findings in this study show that the proportion of Wild Polio virus is higher in the Northern part of Nigeria than in the Southern part. This could be as a result of vaccine refusal in the North. In Northern Nigeria in 2003, the political and religious leaders of Kano, Zamfara, and Kaduna states brought the immunization campaign to a halt by calling on parents not to allow their children to be immunized. These leaders argued that the vaccines were contaminated with anti-fertility agents (estradiol hormone), HIV, and cancerous agents. (Jegede, 2007). Circulation is still occurring mainly in areas that are missed by vaccination teams. The majority of this burden lies in rural, hard-to-read and underserved areas. In the areas where vaccination teams are active, children are still occasionally missed due to pockets of non-compliance, team performance, and

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inadequatemicro-plans.

Further findings reveal that the highest proportion of wild Poliovirus (3.5%) was seen among children aged 24-35months and the least among children older than 60months (1%) 48-59 months age group. It was also observed that wild poliomyelitis occurred equally in boys and girls with no significant association in occurrence. This is consistent with previous studies by Adedeji et al 2012 which reported that poliovirus infection in children occurs equally in boys and girls .(Adedeji et al, 2012).

Wild Polio Virus 1 (WPV1) was also predominant in the Southern part of Nigeria as observed in this study while wild polio virus 3 (WPV3) occurred more in the Northern zones. This is contrary to findings by CDC which states that in countries where poliovirus infection is still endemic, paralytic disease is most often caused by poliovirus type 1, less frequently by poliovirus type 3, and least frequently by poliovirus type 2. Interestingly it can be inferred that between 2009 and 2012 WPV 3 caused more of the paralytic disease in Nigeria.

There was a statistically significant association between age-group, OPV dose, location and the presence of wild status of poliomyelitis. Younger children (2.8%) had a significantly higher proportion of wild Poliovirus compared to older children (1.8%). This may be because older children have a more developed immune system than younger ones. Higher proportion of wild Poliovirus was similarly found among children with zero OPV doses (12.9%) than children who had at least 1 dose of OPV (2.0%) among the AFP cases. This is because the OPV is clinically effective at 57%in children with 1 to 2 doses and 92% in children with greater than 3 doses. This shows that the OPV is protective at different degrees against Wild Poliovirus infection.

More also, the proportion of Northern children with the presence of wild poliomyelitis was about nine times the southern children (3.6% vs. 0.4%). This may be because of vaccine refusal in the North (Jegede, 2007).

However, no statistical association was detected between gender and the presence of wild poliomyelitis (P>0.05) which indicates that the sex of a child is not associated with the probability of contracting the Wild Poliovirus infection.

5.3   Socio-demographic and other factors associated with occurrence of Wild Poliovirus infection

A look at the socio-demographic predictors of the occurrence of Wild Poliovirus reveals that younger children (<35months) are about 2 times more likely to have Wild Polio virus than older children of greater than 35months of age. Moreover, children who had never received Oral Polio vaccination (0 doses of OPV) were found to be about 6 times more likely to have wild Poliovirus than those who had received one or more dose of OPV. This association was found to be statistically significant (P<0.0001). This shows again the effectiveness of OPV against the Wild Poliovirus infection.

In the same vein, children who reside in the Northern part of Nigeria were found to be about 10 times more likely to have Wild poliovirus than those who reside in the Southern part of Nigeria and this also was found to be statistically significant (P<0.0001) and may be associated with the challenge of vaccine refusal in the North. (Jegede, 2007).

This finding is consistent with findings by Deivanayagam et al, 1993 in which an unimmunized child was at 5 times greater risk of developing acute paralytic poliomyelitis than a fully immunized child. (Deivanayagam et al, 1993).

5.4   Clinical Effectiveness of the OPV

The Oral Polio vaccine was assessed and found to be clinically effective. The higher the number of OPV dose the higher the clinical effectiveness. At 1-2 doses the clinical effectiveness was 57%. This increased to 80% at 3 doses and 92% at greater than 3 doses. Children with inadequate (less than 4 doses) OPV vaccination status are therefore not protected and may get infected with wild Poliovirus if exposed.

Vaccine effectiveness among the younger children for 1-2 doses was 70% and this proportion increases with increasing number of OPV doses to 93% at 4 or more doses. However, among the older children, vaccine effectiveness was rather low (5%) at the initial 1-2 doses but went up substantially thereafter to 65% at 3 doses and 89% at 4 or more doses. This suggests that the OPV may therefore not be effective in Northern children who refused the vaccine when young and may later accept it at older age and explains why the vaccine is given early in life, at birth, 6,10 and 14 weeks of age. This further explains why the incidence of Wild Poliovirus is higher in the North than South of Nigeria.

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Clinical effectiveness was found to be higher in Southern Nigeria compared to the North. Vaccine effectiveness in Southern Nigeria was twice that of Northern Nigeria at 1-2 OPV doses. This our findings is consistent with that of Mangal et al 2014 and this poor vaccine efficacy in the North of Nigeria might be a result of a higher incidence of enteric infections, including other Enteroviruses, which might interfere with the response to the vaccine (Mangal et al, 2014)

Other factors affecting Vaccine effectiveness include method of administration of the vaccine, inadequate reverse cold chain system, in appropriate storage among other reasons.

Vaccine efficacy estimates could also be more substantially affected in the North by inaccurate vaccination histories, in view of the frequent rounds of supplementary immunization activities with differing vaccine types. Overall, vaccine efficacy was found to increase with increase in the number of doses.

Lower OPV efficacy would necessitate a higher number of doses to achieve eradication and would support the accelerated introduction of inactivated poliovirus vaccine in high-risk areas to boost immunity to all three serotypes (as outlined in the endgame strategy) and this is a point to be considered especially in the North.

The finding of the Clinical Efficacy of OPV in Nigeria as well is consistent with studies carried out in India (Deivanayagam et al, 1993) in which the OPV was found to be clinically effective(high percentage(95%) and Egypt (kotb et al, 1993). Overall, it can therefore be said that In Nigeria, OPV is still clinically effective.

5.5   Prediction of Optimum OPV dose

Findings from this study revealed that the best cut off points for prevention of occurrence of wild Poliovirus by the OPV doses that maximizes sensitivity and optimizes specificity is 4.0 doses. A cut-off point of 4.0 from this result may be chosen as optimal. At this level, the OPV displayed a sensitivity of 65% and specificity of 71%. Therefore 4 doses are scientifically recommended.

This shows that giving less than 4 doses will not protect against WPV infection and also giving greater than 4 doses. At other possible doses there is great disparity between the Sensitivity and Sensitivity.

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Four doses have therefore been found to be the optimum dose using the results gotten from the receiver operating characteristics curve. What we still need is 4 doses and this is consistent with the present routine vaccination schedule in the country a WHO recommendation. Beyond doubt, this study has achieved a great purpose of confirming the optimum OPV dose required for the prevention of Poliomyelitis in the Nigerian child. This is consistent with the present OPV schedule and can thus be maintained.

It can therefore be inferred that Poliomyelitis still occurs as a result of many factors which may include vaccine refusal, failure to vaccinate and vaccine failure among other factors.

The Government and all Stakeholders therefore need to join hands to ensure the immunization of all children 0- 15 years so that WPV can be eliminated from Nigeria and finally eradicated globally.

5.6 Limitations of the study
Trivalent OPV (tOPV) only was used in the analysis. Other variants such as monovalent OPV (mOPV), bivalent OPV (bOPV) were not considered in the calculation of Vaccine Effectiveness. There was no use of matching controls in the determination of Clinical effectiveness of OPV. Also when Poliomyelitis occurs in 1 child, 200 people might be infected who are not captured in the data used.

5.7 Conclusion and Recommendations
4 doses of OPV have been found to be optimum for prevention of the occurrence of Wild Poliovirus infection. It is therefore recommended that four doses of the oral Polio vaccine should be continued routinely.

The data supports that 4 doses is the optimum dose of OPV required to prevent the occurrence of Wild Poliovirus. This is consistent with the WHO recommendation.

Finally, till further research proves otherwise, 4 doses of OPV should be given to children routinely alongside other routine immunizations.

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