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Poliovirus neutralizing antibody levels among individuals in three regions of Ghana

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Conflict of interest: None declared

SUMMARY
Introduction: Ghana was declared polio-free in 2015 after the last polio case in 2008. We determined the poliovirus neutralizing antibody levels among individuals to identify possible immunity gaps.
Methods: A cross-sectional, hospital-based study was undertaken in Northern, Ashanti and Greater Accra regions of Ghana. Individuals referred for haematology at the teaching hospitals' laboratories were invited to participate in our study. Neutralizing-antibody titers to poliovirus serotypes 1,2 & 3 were assayed by WHO-standards. Antibody titers of ≥8 were considered protective. Bivariate and multivariate analyses were conducted on subject characteristics to assess potential factors for failure to seroconvert. *P*-values < 0.05 were considered statistically significant.
Results: Poliovirus (PV) neutralizing-antibody serotypes 1, 2 and 3 were detected in 86.0% (264/307), 84% (258/307) and 75% (230/307) of samples respectively. 60.1% (185/307) were seropositive for the three poliovirus serotypes. Neutralizing poliovirus antibodies for PV1 and PV2 were higher than for PV3. Seroprevalence of poliovirus-neutralizing antibodies among males (PV1=51.9%, PV2= 51.6% and PV3= 52.6%) were higher than in females. Seroprevalence rates of poliovirus-neutralizing antibodies (PV1, PV2, and PV3) were highest in the Northern region (90%, 81%, and 77%). Poliovirus neutralizing-antibodies (PV1and PV2) decreased with age [p< 0.001]. Low seroprevalence of poliovirus-neutralizing antibodies was significantly associated with low school attendance of mothers (p<0.001).
Conclusion: Our study population has some protection from polio. However, immunity appears to be lower with a higher age or low Mother's education. This may suggest the need for young-adult booster-dose to minimize the risk of wild poliovirus infection.

Keywords: poliomyelitis, seroprevalence, neutralizing antibodies, polio-immunity, Ghana
Funding: WHO Country Office Ghana.

INTRODUCTION
Poliomyelitis is a highly infectious viral disease which can have crippling effects. The disease is caused by the poliovirus serotypes 1, 2 and 3. It mainly affects children who are less than five years of age if exposed to the virus. According to Robert,[1] in developing countries, one out of 200 polio infections paralytic polio is observed, while fatality is normally observed in 5-10% of paralytic polio cases. Fecal-oral route and in a few instances the respiratory transmission are the primary mode of transmission. Most infections of polio are asymptomatic and less than 1% of the infected individual become paralysed. Poor sanitary conditions, high population density and lack of immunization are the major risk factors of polio infection.

Despite the introduction of the Global Polio Eradication Initiative (GPEI) in 1988, polio transmission still exists in three countries namely: Pakistan, Afghanistan, and Nigeria. As at September 28th, 2018, eighteen (18) wild polio cases (WPV) and 53 circulating vaccine-derived polioviruses (cVDPV) had been detected worldwide compared to 11 WPVs and 49 cVDPV within the same period in 2017.[2] Ghana recorded the last cases of poliovirus in 2008.[3]

Seroprevalence is the number of persons in a population who test positive for a specific disease based on serology (blood serum) specimens.

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Important data on the performance of immunization programmes, groups which are susceptible to polio infection and populations at risk of future outbreaks can be obtained from seroprevalence studies.

Low seroprevalence to poliovirus antibodies in a population may contribute to an outbreak of polio in a community. There was an outbreak of polio in Finland between 1984 and 1985 which involved nine cases due to wild poliovirus type 3. Prior to that observation, only 30% of children aged three years who participated in a seroprevalence survey in Finland in the year 1982 had poliovirus type 3 neutralizing antibodies.[4] In a similar outbreak of wild poliovirus type 1 among persons aged more than 15years old in the Democratic Republic of Congo, 2010-2011, the seroprevalence assessment indicated that antibodies against polioviruses 1&3 were lower (<80%) in women aged 15-28 years old.[5]

Evidence of high polio seroprevalence in reducing the risk of poliomyelitis outbreak also abound. In a study of residents in the mainland, Portugal, the seroprevalence of PV1, PV2, and PV3 were 91%, 94.2 and 75% respectively. Portugal had a declaration of polio-free status in 2002.[6] In assessing the immunity status of migrant workers in Israel, the seroprevalence of 99.3%, 98.6 and 99.3 were recorded for PV1, PV2, and PV3 respectively. These results indicated high levels of immunity among foreign workers and this explained the low risk of polio among these groups.[7]

Ghana continues to implement routine and mass immunization that includes polio vaccination. Polio is prevented in Ghana by the use of oral polio vaccine (OPV) which contains three poliovirus serotypes. Ghana currently uses bOPV which contains poliovirus serotypes 1 & 3. Four (4) doses of bOPV (at birth, 6, 10 and 14 weeks) are given in addition to inactivated polio vaccine (IPV) at 14 weeks. IPV does not replace the OPV vaccine but is used with OPV to strengthen a child's immune system and protect them from polio.

The mass polio vaccination which was initiated in 2000 has stalled since 2015 and the Regional Polio Certification Committee had declared Ghana a polio-free country in 2015. Routine polio vaccination coverage has persistently stayed above 90%.[8] Despite the good of impending global eradication, there persist few areas of inherent transmission in Africa (Nigeria) and Asia. A danger of importing wild poliovirus to countries that are almost polio-free therefore still exists.[9, 10]

There were two major polio outbreaks in 2003 and 2008 as a result of immunization gaps.[11]

Furthermore, the country continues to record cases of polio compatibles each year, 26 cases in 2017.[3]

Inadequate service delivery of oral poliovirus vaccine (OPV), suboptimal OPV efficacy, social-cultural beliefs and low seroprevalence to polio neutralizing antibodies may provide some explanations to these observations.[12-14] Low neutralizing poliovirus antibodies may lead to polio outbreak that could result in permanent lameness and possible death. This study determined the seroprevalence of poliovirus neutralizing antibodies serotypes 1, 2 and 3 by evaluating the neutralizing poliovirus antibodies in the Ghanaian population of three regions among the respondents prior to the global switch from tOPV to bOPV. The data provided from this study may serve as an immunity benchmark for the three regions of Ghana against any polio infection to enable identification of the populations at-risk of future polio outbreaks.

METHODS
Study design
A cross-sectional analytical hospital-based study was conducted in three regions of Ghana in 2016. In this seroprevalence study, individuals referred to the laboratory for haematology at the three teaching hospitals partook in the study. The respondents were interviewed with a semi-structured questionnaire extracting data on demographic and polio immunization history. Subsequently, their weight and height were measured. Approximately 2-5 ml of blood was taken from the respondents (children and adults) for microneutralization test. Antibody titers of ≥1:8 were considered protective.

Study areas
This involved the Northern, Ashanti and Greater Accra regions which are located in the three ecological zones of Ghana (Figure1). These regions are the most populated and have the biggest referral and teaching hospitals in Ghana. Patients attending these hospitals come from a wide catchment area with mixed socioeconomic backgrounds. The Northern Region is located in the northern part of Ghana and has the largest land surface area, 70,384 km^2, in Ghana. The region experiences much drier weather conditions than southern areas of Ghana.[15] There are 345 health facilities, a teaching hospital, and over 5,000 government health professionals.[16] The Ashanti Region is located in the middle belt of Ghana. The region covers a total land area of 24, 389 km^2 with a population of 4,780,380 in 2010.[15] There are 548 health facilities, a teaching hospital and 8,200 government health professionals.[16] Located in the southern part of Ghana, the Greater Accra region is the least in terms of size in land area in Ghana with a population of 4,010,054 per the census in 2010.[15]

There are 500 health facilities, a teaching hospital, and over 9,000 government health professionals.[16]

Figure 1: Map of Ghana showing study sites
Legend ⬭ Study Area

Study population
All children less than five years old and adults referred to the laboratories of the three major referral and teaching hospitals (Tamale, Komfo Anokye and Korle-Bu Teaching hospitals) in the Northern, Ashanti and Greater Accra regions of Ghana from 1st of April to July 30th, 2016 were screened for participation in this survey.

Inclusion and exclusion criteria
All children of consenting parents and adults resident in the three selected regions for the past six months were eligible to participate, except those (a) born or residing outside of Ghana; (b) those with serious acute illnesses requiring hospitalization; (c) those diagnosed or suspected of congenital immunodeficiency disorder or an immediate family member, and (d) those with contraindication to venipuncture.

Sample size estimation
The estimated minimum sample size was 274, however, 307 respondents attending or using the laboratories in the three referral hospitals were recruited into the study. This was based on the Fishers formula for calculating sample size for populations >10,000.[17]

$$n = \frac{\left(Z_{\alpha/2} + Z_{1-\beta}\right)^2 p(1-p)}{d^2}$$

The sample size which was aimed at estimating the prevalence of serotypes, p, was computed assuming that p has a normal distribution. If a maximum absolute error of d=0.05 was tolerated with 95% probability ($Z_{alpha/2}$=1.96), assuming a seroprevalence rate (p) of 90%, (Zubairu, 2013. Unpublished) in the population, and applying a power of 0.80 (beta) for each poliovirus serotype leads to a minimum sample, n=274. Adjusting for a non-response rate of 10% (blood provision and availability of mothers or caregivers for interview): n= 307. The sample size was then distributed across the three regions by probability proportional to the size of the population of the study regions.

Screening for the hospital-based seroprevalence survey
The selection of participants for the hospital survey required an initial screening for age (<1, 1-4, 5-14, 15-70 years old) at the respective hospitals in each region. After obtaining informed consent and assent from the participants and the mothers or caregivers who had been sent for laboratory investigations, the study procedure commenced. Screening continued until the sample size of each age group was achieved.

Data collection technique and tools
The technique for data collection was an interview (face to face) using a semi-structured questionnaire as the tool. The study team was comprised of a physician, nurses, laboratory scientists, and field assistants. The study physician explained the purpose of the study to the parents or caregivers and the adult respondents. After obtaining informed consent from all respondents a standardized questionnaire was administered to them through a face-to-face interview. For the children less than five years, vaccination history on routine immunization were extracted from their child health records books, clinic records. Parents or caregivers' recall of doses of vaccines the child had received was acceptable if the parent or caregiver could specify the dose given. Supplemental vaccinations (vaccinations given during national or sub-national immunization days), were obtained through oral histories given by the parent or caregiver. The child's weight and length/height were measured with a digital weighing scale and an infantometer respectively. For all the adult respondents, weight and height were also measured. Body weight was measured on subjects in light clothing and without shoes to the nearest 0.1 kg using with a heavy-duty Seca 770-floor digital scale (Seca, Hamburg, Germany).

Height was measured to the nearest 0.1 cm with a commercial stadiometer in standing position with closed feet, holding their breath in full inspiration and Frankfurt line of vision.

The vertical and horizontal placement of the stadiometer and infantometer were checked by using the carpenter's level and standardized rod at regular intervals. The digital weighing scales were checked using the standardized weights in regular intervals.[18]

Blood collection procedure
Two-five (2-5) ml of venous blood was collected through venipuncture into a vacutainer tube by a phlebotomist. Blood sera were separated within six hours at the hospitals and stored at −20 ºC in a deep freezer. After the data collection, blood samples (sera) were stored in airtight tubes and transported to the Noguchi Memorial Institute for Medical Research for laboratory analysis in a reverse cold chain at a temperature of +2 to +8 ºC.

Quality control measures
Quality control measures consisted of training research assistants, pretesting the questionnaire and procedures, as well as quality checks of data.

Micro-neutralization Test for polio antibodies
Antibodies for poliovirus types 1, 2 and 3 were determined by a microneutralization assay with authenticated Sabin strains, obtained from NIBSC, UK according to the WHO guidelines which measured the ability of a human serum sample to neutralize the infectivity and cytopathic effect of each of the three types of poliovirus on cell cultures in vitro.[19] Sera were heat-inactivated, diluted two-fold serially from 1:8 to 1:1024, and then incubated in duplicate for 3 h at 36 °C with $100 \times 50\%$ tissue culture infective dose (TCID50) of poliovirus antigen. A cell suspension containing 2×10^4 Hep-2C cells/0.1 ml was added. Cell controls and an in-house reference serum sample of known neutralizing activity were included in each batch. After incubation for 5 days, the highest dilution of serum that protected 50% of the cultures was recorded. This was examined with an inverted microscope for the presence of Cytopathic Effect (CPE). A serum sample was considered positive if antibodies were present at a dilution ≥1:8. Titres were computed as geometric mean titres (GMTs).

Data Analysis
Categorical and continuous data were cleaned, coded and entered into Microsoft Excel. Data were then exported to STATA version 13 for analysis. Descriptive analysis of polio neutralizing antibodies was performed by person and place.

Univariate analyses were expressed as frequency distributions, percentages, and mean± SD as appropriate.

Seroprevalence of poliovirus neutralizing antibodies serotypes 1, 2 and 3 were determined as the proportion of poliovirus neutralizing antibodies among the blood (serum) samples. Wilcoxon rank sum test was used to compare differences in median titres by sex and Kruskal–Wallis test was used to compare by age and residence. The association between age and poliovirus neutralizing antibodies was determined by simple correlation analysis with a non-parametric, Spearman Rank correlation test for statistical significance. Binary logistic regression models were used to determine factors significantly associated with seroprevalence with independent variables as sex, education status, age, and residence. $P < 0.05$ was considered significant.

Ethical considerations
Ethical clearance was obtained from the Ghana Health Service Ethics Committee (GHS-ERC 14/11/15) and the Institutional Review Board of Noguchi Memorial Institute for Medical Research (NMIMR-IRB CPN IORG 0000908). Participants voluntarily participated in the study and they (or caregivers) signed written informed consents.

RESULTS
Between April 1st and July 31st, 2016, a total of 307 respondents were enrolled in the survey and 307 serum samples were taken for the analysis. Of the respondents, 153 (49.8%) were females.

Seroprevalence of polio neutralizing antibodies
Neutralizing polio antibodies against poliovirus serotypes 1, 2 and 3 were detected in 86.0% (264/307) [95% confidence intervals CI: 82-90%] for poliovirus type1, 84% (258/307) [95% CI 79.4-87.9%] for type 2 and 75% (230/307) [95% CI 70-80%] for poliovirus type 3 of samples. Approximately, 60.1% (185/307) of the sera of respondents were seropositive for the three polio serotypes and nine (2.9%) sera had no antibodies to the three poliovirus serotypes.

Distribution of poliovirus serotypes neutralizing antibodies by sex, age, and place
The proportion of males compared to females was higher among the seropositive in all the age groups in the three polio antibody serotypes 1 (137/264=51.9 %,) 2 (133/258=51.6%) and 3 (121/230=52.6%) in all three regions. Neutralizing poliovirus antibodies (PV1) was found in females 92.86% (79.77- 97.72) in the Northern region. PV2 and PV3 were recorded highest among males 91.83 % (79.95- 96.95) in Greater Accra and males

83.87% (72.39- 91.16) in the Ashanti region respectively (Table 1).

Children within age group 1-4 years recorded the highest (PV1=29.2%; PV2=27.9%; PV3=28.7%) seropositivity in all polio serotypes (Figure 2). Seroprevalence rate of polio neutralizing antibodies of the three polio serotypes (1, 2 and 3) were highest in the Northern Region: PV1=91.8% (78/85); PV2= 82.4% (70/85) and PV3=77.4% (66/85) (Figure 3).

Distribution of poliovirus antibodies titres that neutralized the three polioviruses with relation to the person (sex, age) and place.
Seroprevalence was analysed descriptively by person and place. There was a significant difference in the median PV1 and PV3 (p-value=0.0514 and 0.0254 respectively) poliovirus neutralizing antibody titre values between males and females. Similarly, there was a significant difference in the median PV1 and PV2 (p-value=0.0001) titre values among the age groups. A statistically significant difference was observed in the median poliovirus neutralizing antibody titre values of PV2 in the three study sites (p-value =0.0046) (Table 2). However, PV1 (p=0.2823) and PV3 (p=0.4151) were not significant.

Table 1 Distribution of polio antibodies that neutralized the three polioviruses with respect to sex and place

| Polio serotypes	Female			Male		
	Northern Region n=42 x % CI (%)	Ashanti Region n=61 x % CI (%)	Greater Accra Region n=50 x % CI (%)	Northern Region n=43 x % CI (%)	Ashanti Region n=62 x % CI (%)	Greater Accra Region n=49 x % CI (%)
PV1	39 **92.86** (79.77- 97.72)	50 **81.97** (70.13-89.80)	38 **76.00** (62.12-85.95)	39 **90.70** (77.42-96.52)	52 **83.88** (72.39-91.16)	46 **93.88** (82.42-98.04)
PV2	35 **83.33** (68.67- 91.94)	52 **85.25** (73.84-92.20)	38 **76.00** (62.12-85.95)	35 **81.40** (66.72-90.52)	53 **85.48** (74.23-92.33)	45 **91.83** (79.95- 96.95)
PV3	32 **76.19** (60.86- 86.81)	43 **70.49** (57.78-80.66)	54 **68.00** (53.77-79.52)	34 **79.07** (64.17- 88.85)	52 **83.87** (72.39-91.16)	35 **71.42** (57.14-82.42)

x=numerator
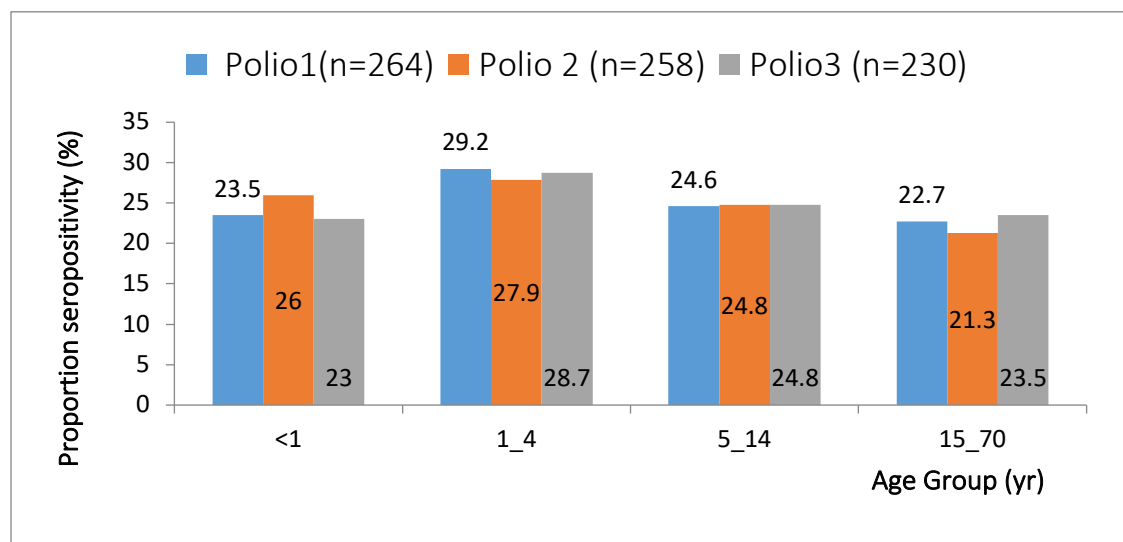
Figure 2 Seroprevalence of poliovirus antibodies among respondents in the three regions, by age group, 2016
Seroprevalence of poliovirus type 1, 2, 3 neutralizing antibodies geographical location
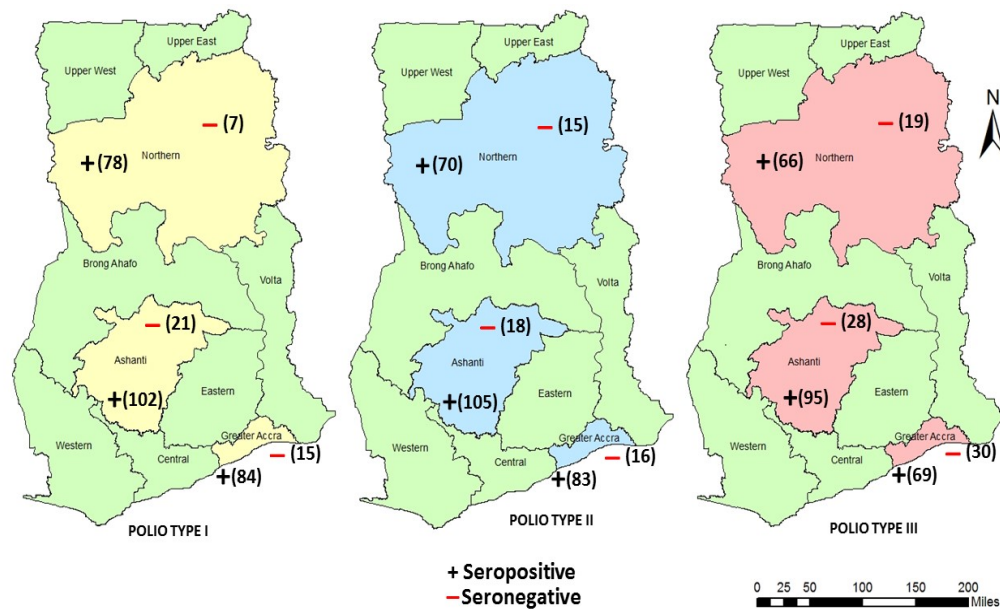
Figure 3 Seroprevalence of poliovirus antibodies among respondents in the three regions, by place, 2016

Table 2 Distribution of respondents' median neutralizing poliovirus antibody titre

Variable	PV1		PV2		PV3	
	Titre (95% CI)	p-value	Titre (95%CI)	p-value	Titre (95% CI)	p-value
Gender						
Male	4.2871 (3.341-5.499)		2.8367 (2.221-3.622)		1.3493 (1.098-1.657)	
Female	2.864 (2.337-3.510)	**0.0514**^{**ł}	2.265 (1.828-2.807)	0.2937	0.9582 (0.809-1.134)	**0.0254****
Age group						
< 1 year	4.629 (3.199-6.698)		4.7911 (3.282-6.994)		1.6055 (1.515-2.2379)	
1-4 years	6.796 (4.847-9.52)		3.243 (2.34-4.493)		1.1300 (0.8664-1.4738)	
5-14 years	2.504 (1.958-3.201)	0.0001^{**ł}	2.1734 (1.651-2.860)	0.0001**	0.993 (0.772-1.279)	0.1995
15-70 years	1.910 (1.471-2.479)		1.222 (0.962-1.552)		0.927 (0.754-1.140)	
Residence						
Northern	3.275 (2.485-4.317)		1.605 (1.270-2.027)		1.226 (0.957-1.571)	
Ashanti	3.118 (2.411-4.031)	0.2823	3.366 (2.539-4.462)	**0.0046**^{**ł}	1.009 (0.831-1.226)	0.4151
Greater Accra	4.301 (3.155-5.865)		2.642 (1.975-3.534)		1.237 (0.947-1.616)	

Median neutralizing polio antibody titre; ł is p-value estimate from Wilcoxon rank sum test; ‡ is p-value estimate from Kruskal Wallis

Age and poliovirus neutralizing antibodies
The age of the respondents had a negative linear relationship with the mean titres of the neutralizing antibodies against the three polio serotypes (Table 3). The presence of neutralizing polio antibodies in the sera of respondents decreased with age.

Table 3 Association between age and mean titres of the neutralizing polio antibodies of the three polio serotypes

Polio serotype	Spearman Rank correlation (rho)	p-value
PV1	-0.2617	< 0.001
PV2	-0.3100	< 0.001
PV3	-0.1099	0.0545

This implies that, generally, as one grows older, the presence of neutralizing polio antibodies decreases, and the opposite trend occurs as participant ages decrease. The PV2 gives the highest negative significant (rho=-0.31, p<0.001) correlation followed by PV1 (rho=-0.2617, p<0.001) and PV3 (rho=-0.1099, p=0.05)

Risk factors for low seroprevalence of Poliovirus antibodies among respondents

The educational status of mothers played a significant role in the presence of antibodies against poliovirus serotype type 1 & 2 among the respondents. With poliovirus serotype 1, the odds of being seronegative among respondents whose mothers had never attended school was 3.9 times (p<0.003) the odds of being seronegative among respondents whose mothers had attended school. A similar picture was found for poliovirus serotype 2 (p<0.001) (Tables 4). This implies that a mother's education is a significant determinant of whether a child will have neutralizing polio antibodies for polio serotypes 1 and 2.

Table 4 Risk factors for low seroprevalence of PV1 antibodies among respondents

Variable	Seronegative (%) n=43	Seropositive (%) n=264	cOR (95% CI)	p-value	aOR (95% CI)	p-value
Mothers schooling status						
Attendant	21(48.8)	182(68.9)	1.0		1.0	
Non attendant	**22(51.2)**	**82(31.1)**	**2.3(1.2-4.5)**	**<0.011***	**3.9(1.59-9.48)**	**<0.003***
Age group						
<1	14(32.6)	63(23.9)	1.0		1.0	
1-4	3(6.9)	74(28.0)	0.18 (0.05 -0.67)		0.29 (0.07-1.08)	
5-14	11(25.6)	65(65.6)	0.76 (0.32-1.80)		1.8 (0.6- 5.3)	
15-70	15(34.9)	62(23.5)	1.1 (0.49-2.44)	**0.0466***	2.6 (0.93-7.6)	**0.0148***
Sex						
Female	26(60.5)	127(48.1)	1.0		1.0	
Male	17(39.5)	137(51.9)	1.5(0.9-2.4)	0.14	1.2(0.6-2.6)	0.48

Non-Attendant mother= A mother who has no formal education

DISCUSSION

It is noted in this study that poliovirus serotypes neutralizing antibodies are 75%-86% of the sera of the respondents. These findings from the study confirm that substantial immunity gaps (differences in the levels of polio neutralizing antibodies) to all three poliovirus serotypes exist in the three (3) regions of Ghana despite intensive efforts to increase immunity levels against polio. With the administration of the polio vaccine and immunogenicity approaching 100% in industrialized countries, only 73% (range 36–99%) and 70% (range 40–99%) of children in developing countries had detectable antibody to PV1 and PV3 respectively after three doses.[20]

In studies conducted in developed countries, neutralizing antibodies in the sera of respondents had shown higher seropositivity compared to those in developing countries. In Germany,[21] England, and Wales,[22] Northern Greece,[23] in Spain,[24] Korea,[25] and in the USA.[26] In Maiduguri Nigeria,[27] North Kano, Nigeria (Zubairu et al., 2013 unpublished), and Zaria[28] recorded lower seroprevalence rates compared to the findings of this study.

Previous polio vaccinations and or infections of wild poliovirus (WPV) together with the polio outbreak in 2008, in the Northern region, may account for the levels of polio population immunity or the antibody levels in the three regions of Ghana. These gaps in immunity levels raise concerns of either primary vaccine failure, that is, lack of initial antibody responses where potent vaccines are used or, failure of the cold chain and the subsequent use of non-potent vaccines in the field.[12-14] The seropositive rate required for maintaining population immunity to polio has not been universally determined by WHO. However, studies have demonstrated that the critical vaccination coverage most likely needed to stop any transmission of poliovirus is 80–85% of the population.[29]

The herd immunity threshold above which one can guarantee the prevention of an outbreak is unclear in Africa and typically for Ghana. However, it has been documented by Sutter,[30] that with population immunity levels (polio neutralizing antibody levels) of 66%–80%, polio outbreaks in developed countries can be prevented. In developing countries with suboptimal sanitation and hygiene with the potential of increased poliovirus (PV) transmission and greater force of infection, wild poliovirus outbreaks could, however, occur with population immunity levels as high as 94%–97%.[30] Therefore, until polio is eradicated globally, many countries including Ghana remain at risk for a poliovirus outbreak.[31]

Evidence exists that low polio neutralizing antibodies in a population may lead to polio outbreak whilst high polio neutralizing antibodies may interrupt transmission of

poliovirus. In an outbreak of wild poliovirus in the Xinjiang Uygur Autonomous Region of China in 2011, a survey indicated that 4.0% of the sample population had no antibodies to the three poliovirus serotypes.[32] In the wild polio outbreak in Finland in 1984 and 1985, wild poliovirus type 3 was implicated. Prior to that outbreak in 1982, a seroprevalence survey revealed that only 30% had neutralizing antibodies to type 3 poliovirus.[4] Serological studies have shown that the outbreak of polio in Kinshasa and Bandundu in the Democratic Republic of Congo in 2010-2011 was likely due to the immunity gap in PV1.[5] In a series of polio outbreak in Northern Nigeria between 2012 and 2013, seroprevalence studies indicated that neutralizing antibody levels among children aged 36–47 months in the study population, was lower than the required levels for poliovirus interruption (Zubairu et al., 2013 unpublished). As long as poliovirus circulation continues anywhere in the world, importations remain a risk and consequently, there remains a limited risk of possible outbreaks among unvaccinated subpopulations.

It is observed in this study that the level of neutralizing polio antibodies of PV3 was the lowest in the sera of respondents. These results are similar to findings in studies in European countries such as Greece,[33] Germany,[34] the Netherlands and Italy.[35] In similar studies in South Africa (Natal/KwaZulu) and other developing countries (Abidjan, Bombay-India, and Cuba) low levels of neutralizing antibodies to PV3 had been documented.[36-39] These observations may be explained by a lower potency of poliovirus type 3 antigens in the vaccine. The low level of neutralizing antibodies of PV3 has also been explained by the fact that PV1 antibodies are due to both vaccination and natural immunity, whereas PV2 and PV3 antibodies are mainly due to vaccine-induced immunity.[40] There is, therefore, the need for a strategy to boost the immunogenicity of PV3 in the polio eradication programme to avoid any future outbreak of polio involving WPV3. In the second quarter of 2016, the Expanded Programme on Immunization (EPI) in Ghana resolved to switch from the administration of trivalent oral polio vaccine to bi-valent. This was in conformity to the WHO strategic plan on polio eradication.[41] This policy direction is on the right path to boost the population immunity levels on PV3.[42] Oral polio vaccine has been indispensable in the polio eradication effort but it is disadvantaged by the fact that during replication of the virus especially in areas with low population immunity, infrequently, reattain the ability to cause paralytic polio.

As wild poliovirus is being eradicated, the need for polio vaccines may outweigh the benefits. The Polio Eradication and Endgame Strategic Plan 2013–2018 (the "Endgame Plan") requires cessation of use of all oral polio vaccines (OPVs) after the eradication of types 1, 2, and 3

polioviruses in order to eliminate vaccine-associated paralytic poliomyelitis (VAPP) and vaccine-derived polioviruses (VDPVs). This phased withdrawal began with the introduction of bivalent OPV (bOPV), containing only attenuated types 1 and 3 polioviruses, in place of trivalent OPV (tOPV), containing attenuated types 1, 2, and 3 polioviruses. This transition from tOPV to bOPV referred to as the "switch" was conducted first because wild poliovirus type 2 (WPV2) was eradicated first, and because type 2 circulating VDPVs (cVDPV2s) have caused the vast majority of polio cases since 2006.[43-.45]

Our study observed that there is a decline in seroprevalence with age. This is consistent with what had been detected in Uruguay,[46] Greece,[23] and South Africa.[36] Contrary to this observation, according to Williams[47] in other studies, neutralizing polio antibodies increased with age. Studies have shown that intestinal immunity to poliovirus wanes over time, therefore individuals could become reinfected and shed poliovirus.[48] The older age groups may contribute to wild polio transmission without clinical symptoms. The World Health Organization has, therefore, recommended that older individuals be vaccinated as part of an outbreak response.[49]

Maternal formal education appears to be a good predictor of the immunization status of their off-springs. This study underscores the importance of maternal education on seroprevalence. It is noted that maternal education has a significant effect on the presence of neutralizing antibodies for the polio serotypes. A lower seroprevalence of neutralizing antibodies depicts lower maternal education.

This argument of lower maternal education supporting lower seroprevalence has been reinforced by similar findings from a study in Northern Nigeria (Zubairu et al., 2013 unpublished). One of the key players in reduction of infant and child mortality is women's education. The higher a woman's level of education, the more likely it is that she will marry later, play a greater role in decision making and exercise her reproductive rights. Her children will tend to be better nourished and enjoy better health.[50]

These findings of the study should be considered in light of limitations. First, there was no immunization history available for adult participants, so it is unclear whether polio sero-immunity was due to past OPV receipt and/or natural immunity.

Secondly, this study is hospital-based, but this limitation may have resulted in an overestimation of seroprevalence of antibody against poliovirus and selection bias, as the children who are not reached by immunization activities may be less likely to visit hospitals.

The results, although not generalizable will give the Ghana Expanded Programme on Immunization (EPI) a fair idea as to the status of immunity in the study population, facilitate innovative strategies to reach the unreached and acquire the needed herd immunity to interrupt the transmission of any future importation of wild poliovirus into the country.

CONCLUSION

This study revealed a moderate level of seroprevalence of neutralizing antibodies to the three polio serotypes with some regional differences. Seropositivity was generally low with increasing age and the mother's education level was crucial to seronegativity. The EPI in Ghana may consider young-adult booster-dose of polio vaccine. The EPI can also consider a one-time NID to mop-up build-up susceptible as a result of missed children since the last NID in 2015. Female child education and career counseling for Junior High School pupils and those older may be intensified by all District Assemblies and by churches.

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