ORIGINAL ARTICLE

Acute Flaccid Paralysis Surveillance in Zambia: Progress towards the Polio End Game

I Mweene-Ndumba[1,2], ML Mazaba[1,2], B Matapo, MR Chirambo, P Mwambi, P Musumbu, F Masaninga, P. Songolo, J Mufunda[1], M Monze[2]

[1]World Health Organization, Lusaka, Zambia, [2]University Teaching Hospital, Lusaka, Zambia

ABSTRACT

Background: In the global polio eradication initiative acute flaccid paralysis cases are followed up two to three months after onset of paralysis to assess recovery of the children. In Zambia AFP cases are followed up regularly but there is no documentation of the clinical and laboratory findings. The purpose of this paper is to document the support WHO country office offers to the follow up of the AFP cases in Zambia to identify gaps which the WHO Country office could address.

Methods: This study used secondary data from a case control study design, conducted and supported by WHO country office, which was aimed at assessing the association of NPEVs with AFP. Particularly this study aims at assessing the presence or absence of residual paralysis and the laboratory findings of the affected children.

Results: A total of 93 cases of, which over 55% were males were included in this study. Majority of the cases were aged between 24 and 35 months (28.4%). Regarding vaccination status, 77% of the cases had received 1 to 4 doses of the Oral Polio (OPV) vaccine. About 62% of the viruses isolated were identified as Cox B, and Echo 3, 6, 7, 11, 12, 14 and 29. Of all NPEVs 37.1% yielded no neutralization pattern. Only 9 (9.67%) cases were followed up; out of which 3 (33.3%) had residual paralysis with one of those with residual paralysis who later died.

Conclusion: AFP surveillance and follow up of cases is carried out in Zambia. However, rehabilitation information of the affected children is not followed up, an issue which WHO country office with regards to the transformation agenda could pursue to ensure that the affected children are adequately supported as a contribution to the polio eradication end game.

INTRODUCTION

Poliomyelitis is caused by poliovirus which is a ribonucleic acid (RNA) enterovirus of the family picornaviridae. Transmission of the poliovirus is through the faecal oral route, after which it enters the blood stream and eventually spreads to the central nervous system where it specifically attacks the motor neurons in the spinal cord.[1,2] The symptoms of poliomyelitis range from fever, malaise, headache, muscle pain, nausea and vomiting to severe symptoms such as acute flaccid paralysis and even fatalities due to respiratory muscle paralysis.[2] Residual paralysis is also one of the severe complications of poliomyelitis. Those most affected are children 0-4 years of age and unvaccinated adolescents.[1] Poliomyelitis is preventable through vaccination which gives a lifelong immunity.[2]

Following a resolution by World Health General Assembly (WHA) and heads of member states in 1988 to eradicate poliomyelitis by the year 2000, member states including Zambia, embarked on active surveillance for acute flaccid paralysis (AFP), as a criterion to identify suspected cases of poliomyelitis.[3,4,5] All stool specimens collected from AFP cases, were sent to the National Polio Laboratory and these are analysed for the presence of enteroviruses according to WHO guidelines.[2,6]

Other than polio virus many studies have reported recovery of non-polio enteroviruses (NPEVs) from the stools of cases with AFP. The studies discovered the following serotypes as most commonly isolated from AFP cases: coxsackie B viruses, echoviruses – 3, 4, 6, 7, 9, 11, 12, 13, 19, 21, 27, 29 and 33.[7-11] The viruses were identified using the micro-neutralization test with pools of antisera recommended for serotyping of common human enteroviruses, although it had been noted that only

Key Words: *Non-polio enteroviruses, Acute Flaccid Paralysis, AFP surveillance, NPEV Serotypes, Polio Eradication Initiative.*

27 out of the 90 common non polio enteroviruses serotypes could be identified by this method.[7,12] Due to the limitation of the test method alluded to above, untypable serotypes of NPEVs were often encountered.[11,13] Other methods such as Enzyme Linked Assay discovered enterovirus 71 (E71) which is implicated in persistent AFP in children.[14] Other researchers recommend the use of molecular methods to adequately identify these viruses and especially if vaccines for NPEV infections were to be considered as these tests provided information on emerging serotypes and their relationship to each other to effectively institute control measures if required.[12,8,15]

The Polio Eradication Initiative (PEI) recommends follow up of AFP cases at 60 to 90 days after onset of paralysis to assess the affected child, and particularly to assess whether the child had residual paralysis or had fully recovered. Many children are reported to have fully recovered while others have remained partially or fully paralyzed for life. Most studies reviewed have confirmed the presence of residual paralysis in a proportion of children amongst whom poliovirus and NPEVs have been recovered from the stool samples, as well as in cases with negative stool samples and have also been reported in cases where untypable NPEVs were isolated from the stool samples. Residual paralysis levels ranged from 7.8% to 39%.[10,11,13] However inadequacies in follow up of AFP cases have also been noted. Not all cases were followed up as recommended and even those that were followed up did not get adequate medical attention.[2,3,16] One would have thought that if a child was found with residual paralysis, measures to alleviate the burden on the child, as well as on the family, would be rendered. In India only cases which had inadequately collected stool specimens and where wild, and Sabin poliovirus was isolated from the stool sample, were considered for follow up.[17]

A qualitative study to explore the care and support rendered to children diagnosed and confirmed with wild polio and NPEV infection, was reviewed. The study participants included parents of affected children, health care providers and community informants. The main findings revealed that there was inadequate support rendered to the children affected with AFP, the health care system was poorly functioning, and the health care providers and families had limited information about available treatment and support for these children.[16] Families highlighted that they felt that health providers visited their homes because they were mainly interested in collecting stool samples rather than the wellbeing of their children.[16] Further the families most affected were those from poor settings living in crowded homes with minimal to no access to medication, information and transportation for the affected child.[16]

In Zambia, follow up of cases has been conducted but very little is known about the outcome of the affected children. Furthermore, there has been no documentation of the laboratory findings in cases found with residual paralysis. Therefore the aim of this article is to document the clinical and laboratory findings of the affected children. This would allow WHO country office identify critical gaps in the AFP follow up system which could be addressed and do things differently from the way they have always been done.

METHODS

This study used secondary data from a case control study design which was aimed at assessing the association of NPEVs with AFP. However, this particular study aimed at assessing outcome of the affected children. The target population for this study was all children in Zambia under 5 years of age.

The cases were children 0 - 5 years old who presented with AFP which was not due to trauma, and who were admitted to a hospital or clinic. The age group was chosen since the literature revealed that children 0-5 years were most affected by AFP. Cases were selected from the national database of the National Virology Laboratory. All cases 0 – 5 years old whose stool samples were referred to the National laboratory from the designated hospitals and clinics were included in the study.

A time-delimited sampling technique was used to select the cases and controls. All AFP cases meeting the study definition that were listed in the database as at 31st December, 2011 and were referred from hospitals included in the study were selected in date sequence, moving backwards in time until the required sample size was realized. A sample size of at least 111 cases was calculated using the Epi-info version 6 “statcalc” functions.

A data extraction form was prepared and utilized to capture the required information on the cases from their hospital folders. The information captured included

demographic data, socioeconomic data, age, sex, date of onset of paralysis, vaccination history, residential area, date stool samples were collected, laboratory virus isolation results of the stool samples and 60 days follow up results of the outcome of their AFP.

All stool samples which were found to contain NPEV had to undergo further testing to determine the NPEV serotype using a standardized microneutralization method which is able to detect coxsackie and echoviruses and which is used in all PEI laboratories. The testing was carried out in cultures of human rhabdomyosarcoma (RD) cell lines at the virology laboratory at UTH, Lusaka.

The generated data was used to describe the laboratory findings of the cases that were followed up after 60 days of onset of AFP. The proportion of cases that had residual paralysis was assessed to determine their NPEV status.

Ethical statement

Permission to conduct the research was obtained from the National Ethics Committee of Zambia and the University of the Western Cape (UWC) Research and Ethics Committee. Since the cases were selected from the national virology laboratory database, authority to use the database was sought from the Ministry of Health and the UTH Virology Laboratory management. Permission to obtain access to participant records was obtained from the managers of the health facilities after the study had been explained to them. The report of this study will be presented to the National Ethics Committee of Zambia, to the PEI management, to the Ministry of Health and to the UTH Virology Laboratory management.

RESULTS

A total of 93 cases of which over 55% were males were included in this study. Majority of the cases were aged between 24 and 35 months (28.4%). Regarding vaccination status, 77% of the cases had received 1 to 4 doses of the oral polio (OPV) vaccine. Table 1 describes the socioeconomic and demographic factors of cases. Of the cases NPEVs were isolated from all age groups except the age group 0 -11 months.

Table 1: Univariate analysis of the socioeconomic and demographic factors

Description	Cases	
Age of child in months	**Total number**	**%**
0-11	13	14.8
12-23	20	22.7
24-35	25	28.4
36-47	18	20.5
48-60	12	13.6
Gender of child		
Male	45	54.9
Female	37	45.1
Vaccination status of child		
Child vaccination status not known or the child received 0 doses of OPV	21	22.6
Child received 1-4 doses of OPV	72	77.4

Circulating Non polio enterovirus serotypes

Identification of the NPEVs was carried out using the neutralization test. As shown in table 2 (annex) 62% of the viruses were identified as Cox B, and Echo 3, 6, 7, 11, 12, 14 and 29. However, of the entire NPEVs 37.1% yielded no neutralization pattern. Out of all the serotypes, 40% were Echo viruses while 22.9% were Cox B viruses.

Table 2: Circulating non polio enterovirus serotypes

NPEV SEROTYPE	Cases	Controls	TOTAL
Cox B	3(3.2%)	5(2.7%)	8
Echo 11	1(1.1%)	0	1
Echo 12	1(1.1%)	0	1
Echo 14	1(1.1%)	0	1
Echo 29	0	1(0.5%)	1
Echo 3	1(1.1%)	0	1
Echo 6	1(1.1%)	3(1.6%)	4
Echo 7	2(2.2%)	3(1.6%)	5
UNTYPED	9(9.7%)	4(2.20%)	13
NPEV Negative	74(79.60)	166(91.2%)	240
TOTAL	93(100%)	182(100%)	275

Follow up of cases 60 days after onset of paralysis

Table 3 below shows the total number of children who were followed up 3 months after the initial onset of paralysis to assess whether the paralysis had subsided or whether it had persisted. However very few cases were followed up after 3 months to check for residual paralysis, as recommended by WHO. The only cases which were followed up were those whose initial stool sample forms were not adequately completed; suggesting follow-up was primarily done for administrative reasons rather than to check on residual paralysis. As a result the follow-up sample was very small and would have a high selection bias. Only 9 (9.67%) cases were followed up; out of which 3 (33.3%) had residual paralysis with one of those with residual paralysis who later died.

Table 3: Follow up results of cases

Follow up results after 3 months	Frequency	Percent
The child died before follow up	1	11.10%
The child had no residual paralysis	5	55.60%
The child had Residual paralysis	3	33.30%
Total	9	100.00%

Of the 3 children that had residual paralysis 1 child had NPEV isolated from the stool samples. The child that died before follow up also had NPEV recovered from the stool sample. Amongst the 5 children with no residual paralysis none of them had NPEVs in their stools. The NPEV isolated from the children who had residual paralysis were untypable and the serotype could not be determined.

DISCUSSION

This study has revealed that 10 out of the 93 cases were followed up 60 days after onset of paralysis based on the inadequacies in the case investigation. This agrees with literature which states that cases were generally followed up because they either had polio virus isolated from the stool samples or there were inadequacies in investigating the case.[16] Of the children followed up in this study, one died before follow up and the laboratory results indicated isolation of NPEV which was untypable. The micro neutralization test method used to type the NPEVs is reported to identify only 27 out of the 90 enterovirus serotypes commonly infecting children. Most studies reviewed have confirmed the presence of residual paralysis in a proportion of children among whom poliovirus and NPEVs have been recovered from the stool samples, as well as in cases with negative stool samples. Residual paralysis has also been reported in cases where untypable NPEVs were isolated from the stool samples. In these studies residual paralysis levels ranged from 7.8% to 39%.[13,11,10] The literature implicates NPEV serotype EN 71 as being the most associated with residual paralysis.[14] This study could not attempt to serotype for this virus due to the limitation of the virus detection methods used. The virus serotype detection methods were limited to those used by the PEI (which does not include EN 71), as this study was conducted using the equipment available in a PEI funded laboratory.

The PEI recommends follow up of children who present with AFP 60 days after the onset of paralysis to assess the persistence of paralysis, or not, as residual paralysis is one of the complications of AFP. This study has shown that only a few cases (10%) were followed up by the health service. Other studies have also confirmed a lack of follow up of cases 60 days after onset of paralysis. As with other studies findings, there was a strong suspicion that children who were diagnosed with AFP were inadequately managed, as one would expect that children diagnosed with AFP are rehabilitated to ease the burden on them and their families.[16] In fact follow up procedures were viewed by families of the affected children as only being interested in stool sample collection for the PEI and not having an interest in the wellbeing of the child.[16] These children's lives are being affected as they usually struggle with daily living activities, are often unable to continue with their education, their family's financial status is adversely affected due to medical costs and costs of transportation to health facilities, and extra time is needed by their caregivers to care for them. Families should be involved by health care staff in the rehabilitation of the child and adequately informed about the procedures to follow in the case of a child developing residual paralysis. Similarly, health care staff should also be well informed about and be given clear guidelines about patient management and mandatory follow up of

cases 60 days after onset of paralysis, by their management and supervisors. Community involvement in follow up management might also be helpful.

CONCLUSION

This study has shown that AFP surveillance is carried out in Zambia and that only 10% of the cases were followed up three months after onset of paralysis. Residual paralysis was reported in 3 out of the 10 cases that were followed up and two of those with residual paralysis had untypable NPEV isolated from the stool samples. However, rehabilitation information of the affected children was not followed up, an issue which could be pursued in other studies.

ACKNOWLEDGEMENT

We extend our gratitude to the Virology Laboratory staff at the University Teaching Hospital, Lusaka for their support, for provision of data on the cases and testing of stool samples. The National surveillance officers for providing follow up findings of cases.

REFERENCES

1. Krugman S, Katz S, L, Gershon AA, Wilfert CM. Enteroviral Infections. *Infectious Diseases of Children*: 1992; (9): 68-85.
2. World Health Organization, 2008. *Acute Flaccid Paralysis Surveillance Field Guidelines*. Regional Office for Africa.
3. Marx, A., Glass, D. J & Sutter, W. R., 2000. Differential Diagnosis of Acute Flaccid Paralysis and its Role in Poliomyelitis Surveillance: *Epidemiology Review,* 22(2): 298-316
4. World Health Assembly 41.28, 1988. *Global Eradication of Poliomyelitis by the Year 2000*. Geneva
5. World Health Organization. 2004. Immunization, Vaccines and Biologicals: *Polio Laboratory Manua*l 4th Edition, 2004.
6. Pan American Health Organization, 1999. Leading causes of Mortality on the United States – Mexico Border: Washington, DC 20037, *Epidemiological Bulletin*, 20(2).
7. Persus, A., Baicus, A., Stavri, S & Combiescus, M., 2009. *Non-polio Enterovirus Associated with Acute Flaccid Pralysis (AFP) and Facial Paralysis (FP) Cases in Romania, 2001-2008*: Cantacuzino Institute, Romania.
8. Dhole T N, Ayayagari A, Chowdhary R, Shakya A K, Shrivastav N, Datta T,*et al*. Enterovirus in Acute Flaccid Paralysis Children of India: Vital Assessment Before Polio Eradication: *Journal of Paediatrics and Child Health* , 2009; 45(7-8): 409 – 413(5).
9. Saeed, M., Zaidi, S. Z., Naeem, A., Masroor, M., Sharif, S., Shaukat, S., *et al*. 2007. Epidemiology and Clinical Findings Associated with Enteroviral Acute Flaccid Paralysis in Pakistan *BioMed Central*. [Online], Available: http://www.biomedcentral.com/1471-2334/7/6 [Downloaded: 02/16/2010]
10. Laxmivandana R, Yergolkar P, Gopalkrishna V, Chitambar SD. Characterization of Non-Polio Enterovirus Infections Associated with Acute Flaccid Paralysis in South-Western India: 2013; *PLOS one*: 8(4):1-9
11. Apostol L N, Suzuki A, Bautista A, Galang H, Paladin F J, Fuji N, et al. *Detection of Non-polio Enteroviruses from 17 Years of Virological Surveillance of Acute Flaccid Paralysis in the Philippines*: Muntinlupa: Philippines2012.
12. Muir, P., Kammerer, U., Korn, K., Mulders, M., Poyry, T., Weissbrich, B., Kandolf, R., Cleator, G. & van Loon, A. (1998). Molecular typing of enteroviruses: Current status and future requirements. The European Union Concerted Action on Virus Meningitis and Encephalitis. *Clinical Microbiology Review,* 11(1): 202-227.
13. Odoom, J. K., Obadai, E., Barnor, J. S., Ashun, M., Arthur-Quarm, J. & Osei-Kwasi, M. 2012. Human Enteroviruses Isolated During Acute Flaccid Paralysis Surveillance in Ghana: Implications for the Post Eradication Era. Full text. In Pubmed: PMID: 23077695. [Online], Available: http//:www.ncbi.nml.nih.gov/pubmed/23077695 [Downloaded: 02/26/2014]
14. Soji, B. O., Olayinka, A. O., Obu, T. H., Mandu, M. B., Nadeba, D. B & Olayinka, O. O. 2007. Non-polio

Enterovirus Implicated in Acute Flaccid Paralysis in Northern Nigeria: *Journal of Medicine and Medical Sciences,* 2(1): 25 – 28.

15. da Silver E, Winkler M T, Pallansch A M. Role of Enterovirus 71 in Acute Flaccid Paralysis after the Eradication of Poliovirus in Brazil. *Emerging Infectious Diseases*. 1996, [Online], Available: http://wwwnc.cdc.gov/eid/article/2/3/96-0312.htm [Downloaded: 02/26/2014].
16. Yotsu RR, Abba K, Smith H, Das A. Support for children identified with acute flaccid paralysis under the global polio eradication programme in Uttar Pradesh, India: a qualitative study. *BMC Public Health*. 2012 Mar 22; 12(1):1.
17. Ministry of Health & Family Welfare. (2005). *Field Guide, Surveillance of Acute Flaccid Paralysis*. 3rd Edition. New Delhi, India