

Laboratory-based Acute Flaccid Paralysis surveillance pre-polio free certification: Indonesia experience, 2003-2013

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Abstrak

Latar belakang: Virus Polio Liar dapat menyebabkan kelumpuhan dan dapat dicegah dengan imunisasi. Untuk memonitor transmisi virus polio liar dilakukan surveilans Acute Flaccid Paralysis (AFP) dan investigasi laboratorium yang telah dimulai sejak tahun 1995 di Indonesia. Virus polio liar Indigenous terakhir ditemukan di Indonesia tahun 1995. Indonesia masih memiliki ancaman importasi virus polio liar dari negara endemis dan mutasi virus polio dari vaksin yang menyebabkan kelumpuhan yang sama seperti virus polio liar. Artikel ini bertujuan untuk memberikan gambaran mengenai surveilans AFP berbasis laboratorium di Indonesia pada tahun 2003-2013 sehingga mengantarkan Indonesia sebagai negara bebas polio pada tahun 2014.

Metode: Data yang dianalisis adalah data kasus AFP seluruh Indonesia periode tahun 2003-2013. Data didapat dari laboratorium jejaring laboratorium Polio di Jakarta, Bandung, Surabaya dan Sub Direktorat Surveilans, Direktorat Surveilans dan Karantina Kesehatan, Direktorat Jenderal Pencegahan dan Pengendalian Penyakit. Data di analisis menggunakan program Microsoft Excel.

Hasil: Sebanyak 305 kasus AFP yang disebabkan oleh infeksi virus polio liar tipe 1 impor ditemukan pada tahun 2005 dan 2006. Terdapat 39 kasus AFP yang disebabkan cVDPV tipe 1 ditemukan di Pulau Madura pada tahun 2005. Virus polio liar tipe 1 hanya ditemukan di pulau Sumatera dan Jawa. Penyebaran Virus polio berhasil dihentikan pada tahun 2006 dan sudah tidak ditemukan lagi hingga tahun 2013.

Kesimpulan: Surveilans AFP berbasis laboratorium yang baik berhasil memantau dan mendeteksi sirkulasi virus polio. Peningkatan kinerja surveillance AFP diperlukan untuk membuktikan terhentinya transmisi virus polio sehingga eradikasi polio secara global dapat diraih. (*Health Science Journal of Indonesia 2019;10(1):8-14*)

Kata kunci: surveilans, laboratorium polio, Acute Flaccid Paralysis

Abstract

Background: Wild Poliovirus can cause flaccid paralysis and can be prevented by immunization. To monitor wild polio virus transmission, Acute Flaccid Paralysis (AFP) surveillance and laboratory investigations was initiated in 1995 in Indonesia. The last indigenous wild poliovirus found at 1995 in Indonesia. Indonesia still has the threat of imported wild polio viruses from endemic countries and poliovirus mutation from vaccine that can cause paralytic as well as wild poliovirus. The aim of this article is to describe the laboratory-based AFP surveillance in Indonesia from 2003-2013 so that it had led the Indonesia certified for polio free in 2014.

Methods: Data analysis performed on AFP cases data from all provinces in Indonesia period of 2003-2014. Data were collected from polio laboratories network in Jakarta, Bandung, Surabaya and the Sub Directorate of Surveillance, Directorate of Surveillance and Health Quarantine, Directorate General of Disease Prevention and Control. Data were analyzed using Microsoft Excel program.

Results: 305 paralysis cases were caused by imported type 1 wild poliovirus infection were found in 2005 and 2006. 39 paralysis cases caused by type 1 cVDPV infection were also found on Madura Island in 2005. Type 1 wild polioviruses only found on the Sumatra and Java island. The wild poliovirus transmission was stopped in 2006 and was no longer found until 2013.

Conclusion: Good laboratory-based AFP surveillance has been successfully monitoring and detecting the circulation of the poliovirus. Improved AFP surveillance performance is needed to prove cessation of poliovirus transmission so that eradication of poliovirus can be achieved globally. (*Health Science Journal of Indonesia 2019;10(1):8-14*)

Keywords: surveillance, polio laboratory, Acute Flaccid Paralysis

Poliovirus can cause poliomyelitis in humans, mainly affects children who have no immunity to the poliovirus. Poliomyelitis can be prevented by immunization which through Expanded Program on Immunization (EPI) started in 1988, the poliovirus transmission has been interrupted. The number of poliomyelitis cases due to wild poliovirus reduced to more than 99% in over 125 countries globally with only 3 endemic countries left nowadays; Afghanistan, Nigeria, and Pakistan. Wild poliovirus type 2 has not been found since 1999 globally while the last case of type 3 wild poliovirus reported in 2012 in Nigeria. Global Polio eradication can be achieved if this condition can be maintained.¹⁻⁶

World Health Organization has implemented four strategies since the eradication program began in 1988, including strategy to increase immunization coverage as well as acute flaccid paralysis (AFP) surveillance and laboratory investigations. The AFP surveillance and laboratory investigation play an important role to ensure the cessation of wild poliovirus transmission. As paralysis was only shown in 0.1- 1% of children infected with the poliovirus, acute flaccid paralysis (AFP) surveillance followed by confirmation with virological laboratory examination needed to assure that there is no paralytic cases caused by poliovirus. AFP surveillance activities which including laboratory confirmation activities were carried out on children under 15 years old through surveillance officers at the District and Provinces Health Service Offices. In Indonesia, this programme have been implemented in Indonesia since 1995.⁷⁻⁹

In Indonesia, indigenous wild poliovirus circulation has not been found any more after 1995. However, Indonesia still faces threat of the wild poliovirus importation from polio-endemic countries as the last previous outbreak in 2005. Moreover polio immunization program in Indonesia utilize Oral Polio Vaccine containing live attenuated vaccines which might become another threat because the vaccine polio virus may experience mutations in the human body (Vaccine Derived Polio Virus/ VDPV) and cause symptoms such as wild polio virus infections.^{1,7,10}

The sensitive and active surveillance in finding AFP cases and laboratory quality is crucial role in ensuring that poliovirus transmission has been interrupted and immunization programme has worked. Documentation of the cessation of the poliovirus transmission is needed in the certification

of polio eradication globally. The data collected may provide evidence of the elimination of the poliovirus and can also be used as a guideline in making plans to prevent and eradicate polio infections. This study provides epidemiological and virological information on AFP cases in Indonesia from 2003-2013 which further gives an overview of polio eradication program in Indonesia before the certification of polio free is obtained. Furthermore, through the data obtained during the period 2003 – 2013, it can be seen the development of the surveillance system in Indonesia in detecting the circulation of wild polio viruses in Indonesia as experiences and a lesson learnt of laboratory networking to prevent poliovirus transmission and achieving polio-free certification including response to the poliovirus outbreak.

METHODS

Study Design

Indonesia has 34 provinces which spread over 5 major islands and thousands of small islands. The health system is managed by the central government in collaboration with local governments with tiered tasks and responsibilities given. This article analyzes AFP surveillance data reported and sent by specimens to the polio laboratory network for the period 2003-2013 before Indonesia was declared polio-free by the World Health Organization. Data analysis covered surveillance activities in finding AFP cases, retrieval and condition of stool specimens.

Acute Flaccid Paralysis surveillance activity

AFP surveillance implements hospital-based and community-based surveillance systems in finding AFP cases. AFP surveillance in Indonesia was performed by Vaccine Preventable Diseases surveillance department Directorate General of Center for Disease Prevention and Control (CDPC) involved all relevant health workers in health facilities to actively find and report acute paralysis cases found in hospitals and health centers and also involved other leaders in the community to capture cases in communities. Specimens should be collected from the AFP cases with at least 2 stool specimens are obtained in 24 hours apart within 14 days after onset and then sent to laboratory accredited by WHO. The specimens should be received in a laboratory with good condition. Acute Flaccid Paralysis surveillance officers in districts will send reports to CDPC Indonesia every month.

Laboratory Investigation

The collected specimens were sent to three polio network laboratories, namely the Center for Biomedical and Basic Health Technology, National Institute of Health Research and Development Laboratory in Jakarta which examined samples from the all the provinces in Sumatera Island region, Kalimantan Island region, Banten Province and DKI Jakarta Province; Biofarma Laboratory in Bandung which examined samples from West Java Province, Central Java Province and D.I.Yogyakarta Province and; Balai Besar Laboratorium Kesehatan (BBLK) Surabaya Laboratory which examined specimens from Sulawesi Island, East Java, Bali, Nusa Tenggara, Moluccas, and Papua Island region. The specimens were examined in the laboratories using procedures established by WHO and results were reported to the Expanded Program on Immunization data in Sub Directorate Surveillance, Direktorat Surveillance and Health Quarantine, DG CDPC as well as to the provincial health offices.⁹

Data Analysis

The data from AFP cases were analyzed combining laboratories and epidemiology data from CDPC which collected between 2003-2013. The data which used in this study is analysed with microsoft excel programme including year, number of AFP cases, number of AFP specimens, the condition of the specimens.

RESULTS

The AFP cases were found by surveillance officers and reported to CDPC and followed by specimens

collection and sent them to the polio laboratory network according to their coverage working area. Figure 1 shows the number of AFP cases reported and specimens collected and sent to the laboratory. The AFP cases reported in 2003 and 2004 were still relatively few, which then begun to increase in 2005, almost reaching twice number of case discoveries in the previous year. The number of cases since 2005 was then relatively consistent until 2013. From the figure it was also seen that less than 10% of cases were reported without specimens sent to the laboratory.

Table 1 shows AFP surveillance performance with the number of specimens received in the laboratory and the condition of the specimen. It appears that specimens in adequate conditions range from 78-90% of all cases found and reported to central surveillance. Table 1 also illustrates the increase in Non Polio AFP rates. Non-polio AFP rate is really the incidence of AFP caused by diseases other than poliomyelitis. Before 2005 there were still around 1/100,000 population of children, whereas in 2005 to 2013 Non Polio AFP Rate increased to >2/100,000 population of children.

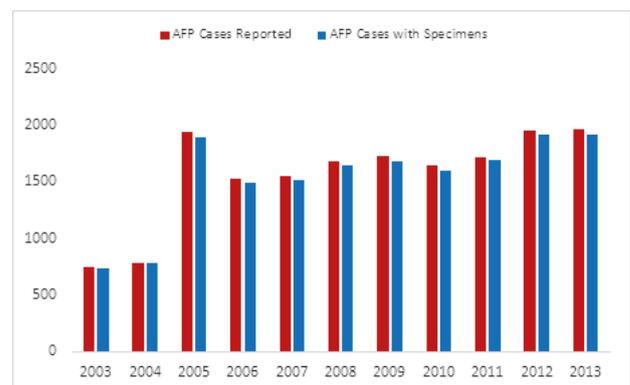


Figure 1. AFP cases trend in 2003 - 2013

Table 1. AFP Surveillance Performance Based on Adequate Specimens and Non Polio AFP Rate

Year	No. of AFP cases Reported	No. of Sample Sent to The Lab	Adequate Specimens		In Adequate Specimens				Non Polio AFP Rate	
			Total	%	Total	1 spc	Without Specimens	Bad Condition		Collection >14 days
2003	749	737	660	88%	89	1	12	31	45	1,22
2004	782	779	705	90%	77	4	3	25	45	1,25
2005	1939	1900	1521	78%	418	37	39	88	254	2,45
2006	1527	1497	1209	79%	318	13	30	101	174	2,46
2007	1557	1516	1263	84%	253	11	41	49	152	2,54
2008	1684	1641	1403	83%	281	16	43	15	207	2,75
2009	1724	1685	1477	86%	247	26	39	13	169	2,81
2010	1641	1601	1385	84%	256	13	40	11	192	2,63
2011	1720	1692	1540	90%	180	6	28	3	143	2,76
2012	1951	1922	1749	90%	202	15	29	7	151	2,77
2013	1963	1922	1722	88%	241	12	41	5	183	2,74

The laboratory tests are virus culture by inoculating specimens to both RD and L20B cell lines followed by identification of Poliovirus using the Probe and Hybridization (2003-2008) and Polymerase Chain Reaction method (since 2009). Table 2 describes the results of viral culture and identification of polio virus in stool specimens from AFP cases. The wild poliovirus were found in Indonesia both in 2005 and 2006. The Vaccine Derived Poliovirus (VDPV) type also detected in 2005 while vaccine Poliovirus were detected every year with the highest was in 2005.

VDPV was originated from vaccine poliovirus and mutated during over time.¹⁰ Vaccine poliovirus type 3 was the most frequently detected amongst the others.

In 2005, there was an outbreak of wild poliovirus in Indonesia. First case of wild poliovirus found in Cidahu district, West Java province in March 2005, which then spread to eight other provinces in Java and Sumatera. Distribution of wild type 1 polio cases in Indonesia in 2005-2006 was shown in figure 2.

Table 2. Laboratory Result of AFP Specimens

Year	Number of Specimen	Vaccine Poliovirus			Wild Poliovirus			VDPV		
		P1	P2	P3	P1	P2	P3	P1	P2	P3
2003	737	1	1	3	0	0	0	0	0	0
2004	779	0	0	1	0	0	0	0	0	0
2005	1900	41	42	58	303	0	0	39	0	0
2006	1497	24	9	13	2	0	0	0	0	0
2007	1516	7	5	9	0	0	0	0	0	0
2008	1641	6	8	4	0	0	0	0	0	0
2009	1685	3	3	5	0	0	0	0	0	0
2010	1601	4	2	6	0	0	0	0	0	0
2011	1692	5	6	20	0	0	0	0	0	0
2012	1922	4	6	11	0	0	0	0	0	0
2013	1922	0	6	9	0	0	0	0	0	0



Figure 2. Mapping of Wild Poliovirus Cases in Indonesia in 2005-2006

DISCUSSION

This paper discusses laboratory-based AFP surveillance activities in Indonesia for the period 2003 - 2013 that represent the period before the discovery of paralysis cases due to imported wild polio virus infection in 2005 until Indonesian polio-free certification was achieved in 2014. AFP cases reported in 2003-2004 were less than the number of cases in the previous year. The highest number of AFP cases was reported in 2005 due to an outbreak of imported type 1 poliovirus which was first

discovered on Cidahu, Sukabumi, West Java. The increased number of AFP cases detected which more than two times from the previous year was due to avoid a paralytic case that escaped from monitoring. All cases of acute paralysis including paralysis of more than 2 months were investigated and reported, followed by collection of stool specimens to expand the possibility of finding paralytic cases due to poliovirus. This strategy was followed with the increase of cases with inadequate specimens in 2005-2006. The number of case findings after 2005

was constant until 2013 may due to an increase in non-Polio AFP rates that followed the rules for finding cases in endemic areas. An increase in cases is needed to prove that there are no more paralyzed cases caused by wild poliovirus as evidenced by the results of laboratory tests.^{9,13-16}

As shown in figure 1 and table 1, not all reported and investigated AFP cases had specimens. There are several reasons of the incompleteness AFP such as the AFP case location was difficult to reach by the health officers (far geographically difficult and lack of transportation), the difficulties of AFP patients for defection. The other reason of incomplete AFP investigation was because the AFP cases detected after 2 months of paralysis symptoms onset, which made the collection of specimens no longer needed. In addition to incomplete specimens collection, more than 65% of the specimens categorized as non-adequate. Inadequate specimens can be caused by specimens collection more than 14 days from paralysis, specimens were not collected, or just collecting and sending one specimen, and the condition of the specimens at arrival in the laboratory were not adequate. Adequate specimens must be above 80% in every single year and this condition cannot be achieved in 2005 and 2006.⁸ The delay in the collection of the AFP specimens might be due to the delays in case finding. The poliovirus was still excreted in 66% -100% in 2 weeks after the onset and the viruses excretion decreases to 15% at the fifth and sixth weeks. Stool can still be collected until the eighth week to catch the possibility of the virus still being excreted. WHO does not recommend to collect AFP specimens after 2 months of paralysis, although the research was conducted in children in China found that the poliovirus was still detected in the stool from AFP cases after the twelfth week.¹¹⁻¹²

Inadequacy of the specimens was also due to collection of only one specimens instead of two. Collecting a pair of specimens is very important because if only 65% of AFP cases showed positive poliovirus detection in both stools, the sensitivity of the poliovirus was reduced in 7% of AFP cases.¹⁷ In addition, around 15% of the specimens which sent to the laboratory were received inappropriate conditions that were not cold or insufficient volume. The main causes of this problem were because the not enough ice packs, the ice pack is not replaced when melted before reach the laboratory. The specimens temperature affects the stability of the virus. The high temperature for a long period causes the viral titre decreases, and will affect the results of laboratory

tests. The poliovirus is stable for 72 hours at 2-8°C until they arrive at the laboratory. Type 1 poliovirus is most affected by increasing temperature. Virus titre decreased by 20% if stored at 22°C for 14 days and 50% if stored at 36°C for 14 days.¹⁸

The risk of occurrence of AFP cases due to importation of poliovirus is very high. Global data for the period of 2003-2014 showed the spread of wild poliovirus cases because of the imported polioviruses were very significant of 53% in 2005, 85% in 2010 and 62% in 2013.²⁰⁻²²

The AFP surveillance system has successfully monitored the wild poliovirus circulation with a finding of 305 cases of AFP caused by type 1 wild polio virus infections in Indonesia in 2005.¹⁹ This poliovirus originated from an African country which transmitted through Indonesian citizens who visit the Middle East.⁹ The poliovirus was first detected in Cidahu West Java and then spread to Banten and quickly spread to the some provinces in Java and Sumatra Island. The immunization response to epidemics through the supplementary Immunization Activity and National Immunization Days in areas affected by outbreaks and areas affected by the outbreak successfully stopped the transmission of wild polio viruses. The last case was found in 2006. Cases are generally found in children living in the vicinity of rivers, areas with high population mobility, low immunization coverage, high population density, poor sanitation. Active and sensitive surveillance can cause cases to be found in certain areas and in large numbers.⁷

Along with the AFP cases due to wild poliovirus, AFP cases due to type 1 VDPV were found in Madura, East Java in 2005. This finding was different from other countries in the world as the type of poliovirus that mutates and becomes VDPV generally is type 2 polio virus.⁵ One of the causes of emergence of VDPV is the low number of children who have immunity to poliovirus.^{7,25} Low immunization coverage was found in 64% of VDPV cases and 50% of cases have never been immunized against poliovirus. VDPV transmission had occurred before the 2005 VDPV outbreak and no cases could be found due to AFP surveillance being relatively less active in the area. Based on 2003 and 2004 data, it was found that AFP surveillance targets before 2005 in that area were still below the WHO recommended target. In addition to Non Polio AFP rates in that year were <1 / 100,000 population (0.4 and 0.7) and adequate specimens were also below 80%. In addition, cold chains that

are not properly managed also cause the stability of the virus to be disrupted during delivery to the laboratory so that the virus were no longer viable and were not detected by laboratory test.^{7,23-26} Based on the specific results of poliovirus isolates in VDPV cases, mutation nucleotide differences between 1.1-1.2% found occurred for 2 years.

The vaccine poliovirus was also found in the stool from AFP cases. Indonesia is still using OPV (Oral Poliovirus) for routine vaccination. Vaccine poliovirus replicates in the human intestine and is excreted through stool. Outbreak Response Immunization (ORI) in outbreak area causes the poliovirus vaccine to be found in the stool of children who have just received immunization in the last 3 months.¹⁵⁻¹⁶ Data of AFP cases from 2003-2013 shows that vaccine poliovirus type 3 was the most frequently found even though some literatures showed that vaccine poliovirus type 2 was most frequently found because of its characteristics that longer circulated and transmitted.²⁷⁻²⁹ Based on Troy et al study in Mexico, shows that vaccine poliovirus type 3 found in 60% in children who recently received OPV. It showed that after direct vaccination, poliovirus type 3 most frequently detected in stool compared to vaccine poliovirus type 1 and 2.²⁹ The vaccine poliovirus can turn into virulent in the human body and causes the same paralysis as wild poliovirus (vaccine associated poliovirus /VaPP). Further investigation is carried out to decide whether the vaccine virus that enters the child's body changes its nature to become virulent and causes paralysis.²⁹

In conclusion, good quality AFP surveillance helps government programmes in detecting the transmission of wild poliovirus and ensuring that wild poliovirus can be stopped transmitting through laboratory evidence. This evidence can be used as a document to achieve polio-free certification and program legacy in maintaining Indonesia free of wild poliovirus. Improved sensitive AFP surveillance performance is needed to provide more quality evidence so that eradication of poliovirus can be achieved globally.

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