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Circulating vaccine derived polio virus type 2 outbreak and response in Yemen, 2021–2022, a retrospective descriptive analysis

Mutahar Ahmed Al-Qassimi^{1*}, Mohammed Al Amad², Ahmed Al-Dar², Ehab Al Sakaf³, Ahmed Al Hadad^{4,5} and Yahia Ahmed Raja'a⁴

Abstract

Background The outbreaks of circulating Vaccine Derived Polio Viruses (cVDPVs) have emerged as a major challenge for the final stage of polio eradication. In Yemen, an explosive outbreak of cVDPV2 was reported from August 2021 to December 2022. This study aims to compare the patterns of cVDPV2 outbreak, response measures taken by health authorities, and impacts in southern and northern governorates.

Method A retrospective descriptive study of confirmed cases of VDPV2 was performed. The data related to cVDPV2 as well as stool specimens and environmental samples that were shipped to WHO-accredited labs were collected by staff of surveillance. Frequencies and percentages were used to characterize and compare the confirmed cases from the southern and northern governorates. The average delayed time as a difference in days between the date of sample collection and lab confirmation was calculated.

Results The cVDPV2 was isolated from 227 AFP cases reported from 19/23 Yemeni governorates and from 83% (39/47) of environmental samples with an average of 7 months delayed from sample collection. However, the non-polio AFP (NPAFP) and adequate stool specimen rates in the north were 6.7 and 87% compared to 6.4 and 87% in the south, 86% (195) and 14%(32) out of the total 227 confirmed cases were detected from northern and southern governorates, respectively. The first and second cases of genetically linked isolates experienced paralysis onset on 30 August and 1st September 2021. They respectively were from Taiz and Marib governorates ruled by southern authorities that started vaccination campaigns as a response in February 2022. Thus, in contrast to 2021, the detected cases in 2022 from the total cases detected in the south were lower accounting for 22% (7 of 32) of compared to 79% (155 of 195) of the total cases the north.

Conclusion A new emerging cVDPV2 was confirmed in Yemen. The result of this study highlighted the impact of vaccination campaigns in containing the cVDPV2 outbreak. Maintaining a high level of immunization coverage and switching to nOPV2 instead of tOPV and mOPV2 in campaigns are recommended and environmental surveillance should be expanded in such a risky country.

Keywords Circulating Vaccine Derived Polio Virus Type 2, Outbreak, Yemen, 2022

*Correspondence:
Mutahar Ahmed Al-Qassimi
maque55@yahoo.com

Full list of author information is available at the end of the article



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As a consequence of the war and humanitarian crisis for about 8 years in Yemen, the health system infrastructure is mostly destroyed, routine immunization (RI) coverage is low [11], and significant numbers of vaccine-preventable disease outbreaks such as diphtheria and measles are reported.

Case ascertainment and definition

In 1998, the Yemeni Ministry of Health, with the support of World Health Organization (WHO), established the Acute Flaccid Paralysis (AFP) surveillance system to detect paralytic poliomyelitis.

Despite the political division in the country, the system is still unified and functioning as a national system for all parts of Yemen. The activities of the AFP surveillance system, as described in the previous study [8], include AFP case detection, reporting, investigation, sample collection, active search, and flow-up assessment of AFP cases after 60 days of paralysis onset. The WHO definition for VDPVs was used; an AFP case with genetic sequences from at least one stool sample shows Sabin-related poliovirus divergence ($\geq 6\%$ nucleotides (nt) in genomic part VP1) for PV type 2. Epidemiological information on source patients and isolates was collected by surveillance staff. Epidemiological case investigation for each AFP case is conducted and the data of cases, collected samples, and results are kept at national AFP surveillance in the general directorate for disease control and surveillance.

Environmental surveillance for poliovirus

The establishment of environmental surveillance in the country was planned to start in 2017, but due to the crisis situation, it started in July 2021. Three governorates, including Sanaa City, Al-Hodeida governorates (located in the north) and Aden governorate (located in the south), were selected and specimens from the main swage stations were started on a monthly basis. The bag-mediated filtration system (BMFS) method, which is a new environmental surveillance tool, was used. Sample volumes of up to 6 L of wastewater using gravity filtration were collected. This method offers higher sensitivity as it samples a large volume; it is able to sample volumes of wastewater 10 to 20 times greater than the two-phase method, and the small filters are easier to ship from remote and challenging environments than liquid samples. The use of preservatives on the filter reduces the need for immediate processing when the filters are received at a reference laboratory [12, 13].

The collected virocap filters are sent to the national Center for Public Health Laboratories (CPHL), where preservation agents are added to them and stored in the cold chain until the time of shipment.

Data management and analysis

The surveillance data of the AFP surveillance program, data of environmental surveillance, reports related to cVDPV2 outbreak and response measures, e.g. data of vaccination campaigns in each region were used. The data included demographic variables for confirmed cases (age, sex, location), date of paralysis onset and vaccination status of confirmed cVDPV2 cases. Date of environmental sample collection and results. Dates of implemented vaccination campaigns, targeted population, places and coverages.

A retrospective descriptive study of all children affected by cVDPV2 during 2021–2022 was performed.

Epi-Info version 7.2 was used for data analysis. A descriptive statistic: frequencies and percentages were used to compare the characteristics of confirmed cases from southern and northern governorates. The average delayed time for lab confirmation as the difference in days between the date of sample collection, shipment, and receiving lab result was calculated.

Results

Detection of vaccine-derived polioviruses cases

Referral lab results on 22 November confirmed the isolation of a new emergence of VDPV2 from an AFP case (the index case), reported on 31 of August 2021, from Thubab district, which is located in the part of Taiz governorate that is ruled by southern authority. It was a female aged 108 months (9 years), she had not been vaccinated against polio and experienced onset of paralysis on 30 August 2021. The second isolation, genetically linked to the first one, was from a 26-month-old girl reported from Marib district, Marib governorate. The child had also not been vaccinated against polio and experienced onset of paralysis on 1st September 2021, which indicated a new emergence of cVDPV2 in the country.

Up to December 2022, a total of 227 lab-confirmed cVDPV2 cases were reported from 19/23 Yemeni governorates, including 7% (16/227) reported from 2 governorates (Tazi and Marib), of whom some districts were partially ruled either by north or south authorities, 9% (21/227) reported from 6 governorates ruled by south authority and 84% (190/227) reported from 11 governorates ruled by north authorities. Generally, 86% (195/227) of the confirmed cases were reported from the northern governorates, and 14% (32/227) were reported from the southern governorates.

The first detected case (Index case) in Taiz governorate was followed by four cases reported in September; one case was reported from the same governorate, and three cases were from Marib, Abyan and Aden governorates, which are ruled by south authority. The first confirmed cVDPV2 cases from northern governorates were

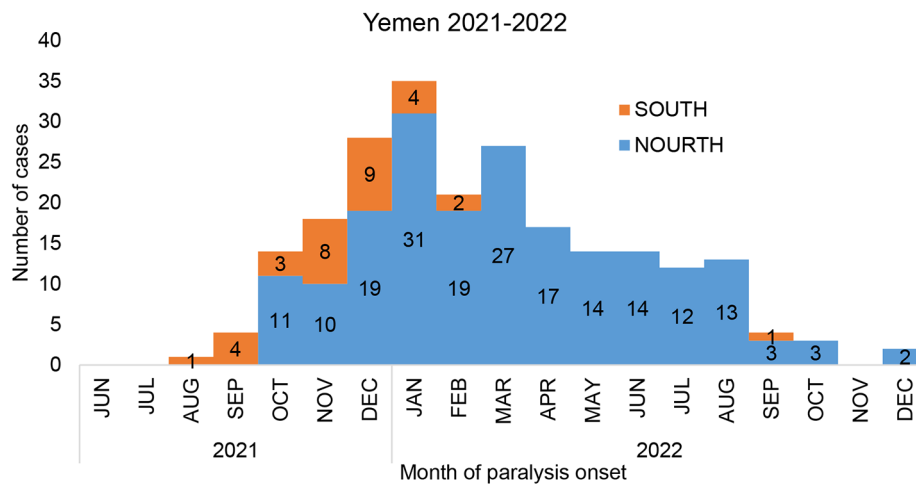


Fig. 2 Epi curve of confirmed case by month of paralysis onset, Yemen 2021-2022

Table 1 Characteristics of reported cVDPV2 cases from north and south Yemen, 2021–2022

Cases of cVDPVs Characteristics	Whole country		North		South	
	No.	%	No.	%	No.	%
Year						
2021	65	29%	40	21%	25	78%
2022	162	71%	155	79%	7	22%
Age group						
< 5 Ys	207	91%	179	92%	28	88%
> 5 Ys	20	9%	16	8%	4	12%
Sex						
Male	142	63%	124	64%	18	56%
Female	85	37%	71	36%	14	44%
IPV in RI						
Zero dose	187	82%	158	81%	29	91%
One dose	40	18%	37	19%	3	9%
Main AFP surveillance indicators						
Years	NPAFP rate	%ADEQ	NPAFP rate	%ADEQ	NPAFP rate	%ADEQ
	6.6	87.5%	6.7	87%	6.4	88.5%
2021	5.5	88%	5.6	87%	5.3	89%
2022	7.7	87%	7.8	87%	7.4	86%

NPAFP; non polio acute flaccid paralysis/100,000 population < 15 years, ADEQ; # of AFP cases with 2 stool specimens collected \geq 24 h apart and \leq 14 days of onset, RI: Routine Immunization, IPV: Inactivated Polio Vaccine

reported from another part of Taiz governorate that is ruled by north authority (supplementary Table 1).

The confirmed cVDPV2 cases from Northern governorates started in October 2021, (two months of the index case) when the confirmed cases had increased to reach 14 cases (3 cases from the South vs. 11 cases from the north). The detected cases reached the highest peak of the Epi curve in January 2022 with 35 cases (4 from the south vs. 31 from the north).

By February 2022, the number of detected cases decreased to 21 cases (2 from south vs. 19 from north). In March 2022, the number of reported cases from south

reached zero cases while 27 cases were reported from the north (Fig. 2).

Out of the total 227 confirmed cases, 29% (65) were reported in 2021, 91% (207) were below 5 years old, the median age was 18 months, ranging from 3 to 156 months, 63% (142/227) were males and 82% (187) had zero doses of IPV. The confirmed cases from the North compared to the confirmed cases from the South accounting for 21% (40 of 195) and 78% (25 of 32) of the reported cases in 2021 compared to 79% (155 of 195) and 22% (7 of 32) of the reported cases in 2022 from the north and south, respectively. (Table 1)

been vaccinated at any of the three rounds implemented in the South.

In contrast, the number of confirmed positive cases in the northern governorates continued to fluctuate between increases and decreases, reaching 2 cases in December 2022. (Fig. 4)

Discussion

This study describes the cVDPV2 outbreak in one of the Eastern Mediterranean conflict countries, such as Yemen, where the confirmed cVDPV2 cases accounted for one-third of the global reported cases in 2022 [14]. The study provides an example of conflict countries where the outbreak is exacerbated by many contributors, such as health system collapse, incapacity for testing and difficulties in samples transportation [11, 15].

The finding indicated a new emergence of VDPV2 outbreak in Yemen, which was confirmed in 2021. Yemen switched from tOPV to bOPV in April 2016 and the last confirmed case of VDPV2 was ambiguous type aVDPV2 in June 2016. The new emergence of cVDPV2 after nearly 5.6 years of the last confirmed case might be due to a vaccine virus (most often mOPV2) that probably entered the country through population movement from Horn of Africa countries (HOA), where since year 2018 large-scale campaigns with mOPV2 in response to cVDPV2 have been implemented, and from January to December 2018 about 834,665 migration movements from HOA to Yemen were reported [16–20]. The huge influx of migrants from Ethiopia and less extended from Somalia to Yemen can carry a risk of polio viruses transportation and might be the main contributor [21].

Our result showed the outbreak of the new emergence VDPV2 started in the southern part of Yemen, particularly in Thubab district and within a month spread to

three governorates in the south and within two months with a higher number of cases to another part of Taiz governorate and four governorates ruled by northern authorities. This finding could be attributed to the coastal location of Thubab district, which could be used as a transit point for Ethiopian migrants who then either move to the southern or northern governorates. The higher number of cases in the northern governorates could be attributed to the higher population of under-vaccinated children and the prolonged circulation of the virus in the northern governorates compared to the southern governorates.

The result indicated that by the end of February 2022, i.e., six months after the first confirmed case, cVDPV2 cases were reported from 19 governorates. The emergence and circulation of cVDPV2 within this short period might be explained by the decline of intestinal mucosal immunity levels against serotype 2 poliovirus after the switch from tOPV to bOPV in 2016.

Similar to the result of the previous study, which revealed a delay in lab confirmation [8] the result of this study showed a delay of 86 days between the detection of the second linked case and the confirmed lab result and 176 days between the lab result of the second isolate and the implementation of the first round of vaccination campaigns in the south.

The findings in this study showed that, in contrast to the north governorates, the majority of confirmed cases were detected in 2021 and no cases were detected after February 2022, while the majority of reported cases from the north were detected after February 2022. The difference is attributed to the implementation of two large-scale house to house vaccination campaigns in south governorates. This result indicated evidence for the

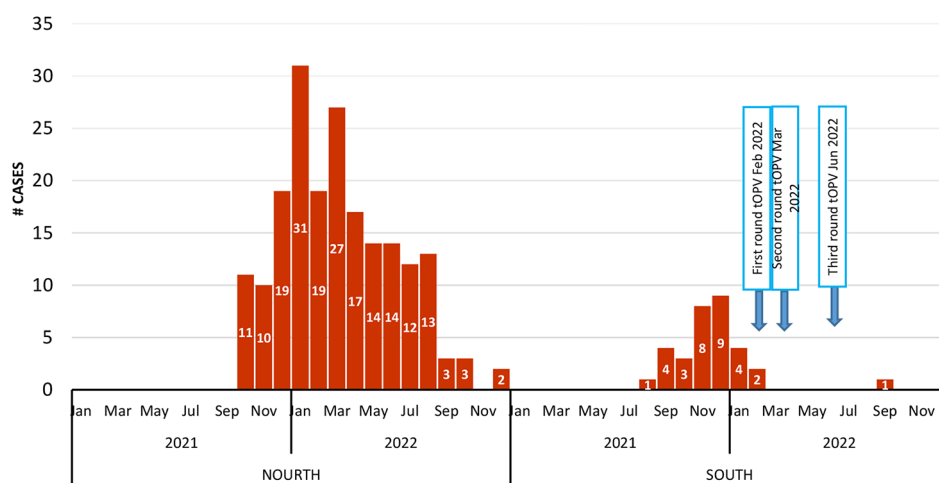


Fig. 4 Time distribution of cofirmed CVDPV2 cases and implimented vaccination campaigns, Northern and Souther Yemen 2021-2022

effectiveness of the house-to-house vaccination strategy campaigns to stop the circulation of cVDPV2.

While most of the countries affected by cVDPV2 outbreak used mOPV2 and recently nOPV2, the country chose tOPV3 in response because the country suffered from cVDPV1 outbreak in 2020–2021.

nOPV2 is a more genetically stable vaccine than Sabin OPV2, which was created to reduce the possibility of reversion to neurovirulence.

The use of nOPV2 in outbreak response to cVDPV2 is required for a timely response, high quality, and sufficient reach [4, 22].

Our result showed only four governorates haven't reported cVDPV2 cases: one in the north and three in the south. Ramah governorate in the north, which is a hard to reach, mountainous area with difficult terrain and is not easy to access, has lower population movement compared with other northern governorates. The three governorates in the south, including Soqatra, which is an island, Al-Mahra, which is an eccentric desert governorate and Hadrmout Al-Muklaa have low population movements. Furthermore, the implementation of three rounds of house-to-house campaigns in the southern governorates may contribute to stopping the circulation of virus there.

The majority of lab-confirmed cVDPV2 from both north and south governorates had zero doses of IPV, this indicates insufficient routine immunization coverage.

The result also showed 18% of children who received one dose of IPV were affected. This might be due to the fact that one dose of IPV gives only 33%, 41%, and 47% protection for serotypes 1, 2, and 3, respectively [15]. This finding has shown a big challenge in the immunity profile of children against type 2, thus IPV routine vaccination should be administered in three doses to achieve full protection of children all around the world [23].

Our result showed the sensitivity of ES, even with the prolonged delay of testing (221 days) and spread of the virus in most governorates. The isolation of the virus from all ES since August 2021 up to November 2022 revealed a sensitive ES and an explosive outbreak, so the delay in ES testing should be addressed and managed to improve the timeliness of response procedures.

Our findings showed that the cVDPV2 virus was isolated from stool samples and ES in Yemen, which is consistent with the findings in Egypt and Djibouti [4].

Several countries have reported that polioviruses (VDPVs) circulating in the population have also been found in environmental sewage. For instance, in Sudan in September 2020, the virus was detected both in the AFP cases and sewage in Egypt [24]. Similarly, the cVDPV2 virus responsible for a large outbreak in Afghanistan has been identified in sewage in two districts of Iran and in two cases of acute flaccid paralysis (AFP) in Tajikistan

[17, 24]. These findings suggest that environmental surveillance can be an effective tool for identifying circulating VDPVs outbreaks and closing gaps in detecting polioviruses during the endgame of polio eradication.

There are some limitations to this study. It is based on secondary data collected by surveillance staff. It did not address the immediate response to the confirmed cases as it was late due to delayed lab confirmation and limited due to the security situation. Although there are many limitations, the study provided information on the impact of providing a large-scale campaign to stop such an outbreak and provides an example of the effectiveness of large-scale vaccination as containment measures for cVDPV2 in conflict areas.

Conclusion

After nearly 5.6 years since the last confirmed case of ambiguous type aVDPV2, a new emerging VDPV2 outbreak was confirmed, and within six months of the first confirmed case. Many factors have been contributed to the spread of cVDPV2 to the majority (19/23) of governorates: the low population immunity as an impact of insecurity on immunization coverage, the delay of response as a consequence of lab confirmation delay. However, six-month delay in implementing vaccination campaigns as a response to the outbreak, due to insecurity issues the vaccination campaigns were implemented only in the southern governorates but not in northern governorates. As a result, no more cases were detected in the southern governorates while the majority of confirmed cases were detected in the northern governorates.

Use of mOPV2 in HOA countries and high population movement across Yemen was the source of SL2 that diverged and circulated in the country in children with low immunity against this type, so changing to nOPV2, which is more genetically stable, in response campaigns will decrease this risk [19, 25, 26].

The cVDPV2 was isolated from environmental samples after an average of 7 months after sample collection. Environmental surveillance is an effective tool in polio eradication for early detection and monitoring during and after the outbreak, but the specimen's transportation is still a big challenge in Yemen.

Recommendations

Maintaining a high level of immunization coverage is essential to preventing the emergence and circulation of VDPVs. Achieving high levels of routine vaccination coverage with second doses of IPV all over the country. Environmental surveillance samples transportation should be radically resolved, and the system should be expanded in such a risky country. Timely and large-scale immunization campaigns should be implemented in response to cVDPV2 outbreaks, with the use of nOPV2 instead of

tOPV and mOPV2 in SIAs to decrease the risk of the new emergence of VDPV2.

Advocacy, community leadership mobilization and fighting rumors against immunization should be utilized, especially in the northern part of the country.

Abbreviations

AFP	Acute flaccid paralysis
aVDPV	Ambiguous vaccine-derived poliovirus
bOPV	Bivalent oral polio vaccine
BMFS	Bag Mediated Filtration System
CDC	Centers for Disease Control and Prevention
cVDPV	Circulating vaccine-derived poliovirus
ES	Environmental Sample
ITD	Intratypic differentiation
iVDPV	Immunodeficiency-related vaccine-derived poliovirus
IPV	Inactivated Polio Vaccine
GPEI	Global Polio Eradication Initiative
HOA	Horn of Africa
mOPV2	Monovalent Oral Polio Vaccine type 2
NPEC	National Polio Expert Committee
nOPV2	Novel Oral Polio Vaccine type 2
Nt	nucleotides
ONPL	Oman's National Polio Lab
OPV	Oral polio vaccine
RI	Routine immunization
SIAs	Supplementary activities
SL1&SL3	Sabin like 1 and 3
SOPs	Standard Operational Procedures
tOPV	Trivalent oral polio vaccine
VDPV1,2	Vaccine-derived poliovirus type 1, 2
WHO	World Health Organization

Supplementary Information

The online version contains supplementary material available at <https://doi.org/10.1186/s12879-024-09215-1>.

Supplementary Material 1

Supplementary Material 2

Author contributions

Authors' contributions: MAA, MA, AD, EA, AH and YR All authors cooperated in this work MAA contributed to the conception and design of the study, literature search and wrote the first draft manuscript. MA, AD, EA contributed to data collection, performed the statistical analysis writing the draft manuscript. AH and YR contributed to revised the final draft manuscript. All contributed to interpretation and writing. All authors read and approved the final manuscript.

Funding

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Data availability

All relevant data are presented in this paper, and more information can be provided upon reasonable request from the corresponding author.

Declarations

Ethics approval and consent to participate

As these data were collected by surveillance staff, and the use of such data is part of the national surveillance activities, and due to retrospective nature of the study official permission for health authority was obtained. The approval for the study was waived by (Ministry of Public Health and Population) Ethics committee, and the need for informed consent was waived by (Ministry of

Public Health and Population) ethics committee. The authors confirm that all methods were performed in accordance with the relevant guidelines and regulations in the county. The study did not involve experiments on the human subject or human participants under the age of 18 years. No human studies are presented in this manuscript.

Consent for publication

Not Applicable.

Competing interests

The authors declare no competing interests.

Author details

¹National Polio surveillance coordinator, Yemen Ministry of Public Health and Population, Sana'a, Yemen

²Department of Community Medicine, Faculty of Medicine and Health Sciences, Sana'a University, Sana'a, Yemen

³General Director for Diseases Control and Surveillance, Yemen Ministry of Public Health and Population, Sana'a, Yemen

⁴Faculty of Medicine and Health Sciences, Sana'a university, Sana'a, Yemen

⁵Yemen National Certification of polio eradication Committee chairperson, Sana'a, Yemen

Received: 2 November 2023 / Accepted: 12 March 2024

Published online: 15 March 2024

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