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Review Article

Vaccine-Derived Poliovirus: Epidemiology, Types, Global Response and Future Prospectives

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ABSTRACT

The genetic biodiversity of Polio virus transmission is a key indicator for epidemiologists to examine the transmission patterns of individual virus lines or families. In 2022, the identification of polio cases in many regions of the world free from the disease for several decades, gained significant attention due to their high-profile nature. These detections understandably raise concerns and necessitate appropriate management and response. However, their significance extends beyond individual incidents, serving as a stark reminder of the potential consequences if global polio eradication efforts fail to the worldwide resurgence of the disease. In August 2020, the World Health Organization (WHO) certified the African region as free from wild poliovirus as the oral poliovirus vaccine (OPV) provides durable protection by inducing long-lasting humoral immunity. One notable characteristic of OPV is its capacity to not only immunize the recipients but also reach and safeguard unvaccinated individuals close to the vaccinated ones, extending its impact beyond the immediate recipients. However, the continued use of the OPV, which contains an attenuated virus, has the potential to undergo mutations, resulting in the emergence of vaccine-derived poliovirus (VDPVs) strains particularly, serotype 2 (VDPV2) causing poliomyelitis. In this review, we focused on epidemiology, highlighted virus classifications, understood the features and transmission patterns of vaccine-derived polioviruses, and discussed the global protective and up-to-date control measures that should be undertaken to limit the spread of VDPV2.

Keywords: *Poliovirus;vaccine-derived poliovirus; oral polio vaccine (OPV); vaccine-derived poliovirus serotype 2.*

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1. Introduction

Poliomyelitis is an ancient disease with records dating back to around 1350 BC, as depicted in an Egyptian stele that portrays a young man suffering from characteristic symptoms such as asymmetric flaccid paralysis and leg atrophy. Additional accounts of the disease can be found in literature from the 17th and 18th centuries and the mid-19th century brought about significant societal changes with the advent of the Industrial Revolution, leading to increased urbanization and improved living conditions in Europe and North America. Coinciding with these transformative shifts was the emergence of more frequent and larger-scale outbreaks of poliomyelitis. Starting in the late 1800s, outbreaks became prevalent in various European countries as well as the United States **[1]**. A major advancement in the understanding

and management of poliomyelitis took place when scientists made an important observation regarding the cultivation and growth of the poliovirus in laboratory cultures using human embryonic tissues. This discovery proved to be a critical step in the examination of the virus and the development of diagnostic techniques and strategies to combat the illness **[1]**. Since April 2016, an important modification has been made to the OPV by eliminating the serotype 2 component. This significant action was taken to prevent the occurrence and spread of VDPV2 and to reinforce global endeavors in eradicating all serotype 2 polioviruses. Consequently, children born after this date now face limited immunity, giving rise to concerns about the potential for worldwide transmission **[2]**. In August 2020, the WHO certified the African region as free from wild poliovirus **[3]**. The OPV vaccine provides durable protection against poliomyelitis by inducing long-lasting humoral immunity. One notable characteristic of OPV is its capacity to not only immunize the recipients but also reach and safeguard unvaccinated individuals close to the vaccinated ones, extending its impact beyond the immediate recipients **[4]**. The collaboration among the Global Polio Eradication Initiative (GPEI), WHO, and Ministries of Health (MOH) has played a critical role in the ongoing efforts to eliminate poliovirus. However, the continued use of the OPV vaccine, which contains an attenuated virus, has presented challenges. This is because the vaccine has the potential to undergo mutations, resulting in the emergence of vaccine-derived poliovirus (VDPS) strains **[5]**.

2. History of vaccine development

John Enders, Thomas Weller, and Frederick Robbins of Boston Children's Hospital achieved a breakthrough in 1949 when they successfully cultured poliovirus in human tissue. Their groundbreaking work was acknowledged with the Nobel Prize in 1954. Soon after, in the early 1950s, US physician Jonas Salk developed the first effective vaccination. Salk tested his experimental killed-virus vaccine on himself and his family in 1953, and 1.6 million children in Canada, Finland, and the United States a year later **[6]**. Albert Sabin, a physician and microbiologist, developed a second type of polio vaccine, the OPV vaccine. Sabin's vaccine was live-attenuated and could be administered orally, as drops, or as a sugar cube. With the Salk vaccination widely used by the late 1950s, enthusiasm for screening this new type of vaccine in the United States was limited **[6]**.

The OPV vaccine revolutionized large-scale vaccination programs due to its convenient mode of administration. Hungary took the pioneering step of introducing OPV in December 1959, followed by Czechoslovakia in early 1960. Remarkably, Czechoslovakia became the first country worldwide to successfully eradicate polio, demonstrating the effectiveness of OPV in combating the disease on a national scale **[6]**.

3. The Global Polio Eradication Initiative

The GPEI was Launched in 1988 after the World Health Assembly passed a resolution to eradicate polio. The collaborative efforts of the GPEI and its partners have achieved remarkable progress in safeguarding the global population against the devastating impact of polio **[7]**. Since the GPEI's inception, the global incidence of polio has decreased by a prevalence of about 99.9%. This incredible invention has enabled about 16 million people who would otherwise be disabled and has saved the lives of more than 1.5 million people who would otherwise have died from the disease **[8]**. Worldwide, the incidence of polio had dropped by 99% in the year 2000, compared with an estimated >350,000 cases recorded from 125 endemic countries in 1988. Three WHO Regions (the Americas, the Western Pacific, and Europe) had been declared polio-free by 2002 **[8]**. The GPEI and WHO announced a

protocol for the detection and monitoring of poliovirus secretion either in the environment by collecting samples from sewage or water treatment or suspected Acute Flaccid Paralysis (AFP) cases, contacts, or even healthy children.

4. Host factors/processes involved in Poliovirus attachment, entry, and internalization

Poliovirus is single-stranded positive sense linear RNA, it is a non-enveloped virus spherical shaped and icosahedral symmetry: spherical in shape with an icosahedral symmetry. Its capsid consists of 60 subunits and 4 viral proteins (VP1, VP2, VP3 and VP4). Poliovirus is attached to (CD155) which is an immunoglobulin-like molecule **[9]**. The antigenic types are Poliovirus type 1, type 2, and type 3. It can be transferred mainly via the feco-oral route and is less common by inhalation, or by conjunctival contact **[9]**. During the infection process, the poliovirus demonstrates a rapid replication cycle, typically taking around 8 hours from the initial infection to the release of progeny virions through host cell lysis. This efficient replication mechanism leads to the generation of substantial amounts of viral proteins and genomes during the infection phase **[10]**. This will result in viremia and spread to the central nervous system, resulting in neurodegeneration.

5. Clinical manifestations

Acute flaccid paralysis (AFP) is clinically described as an acute onset of limb weakness with different degrees of autonomic and somatic nervous system dysfunction **[11]**. This disorder may adversely impact several sections of the body, including the spinal cord, peripheral nerves, neuromuscular junctions, and muscles. The surveillance system was designed to identify clinically suspected cases of poliomyelitis and subsequently monitor them using laboratory tests to confirm or rule out the diagnosis of poliomyelitis caused by the wild or vaccine-derived poliovirus **[12]**.

6. Characterization of the pathogen

According to WHO standards, the poliovirus detection approach is based on collecting stool samples, which is more complicated because sampling requires collecting two samples separated by 24 h. Furthermore, wastewater samples before treatment are used to monitor wellness and vaccination coverage during campaigns to detect the public health of specific groups of people. The collection of samples is dependent on selecting the best location for collecting sewage samples. After processing, the samples will be inoculated on a specific cell line and observed for any cytopathic effect (CPE). The L20B cell line, which originates from (mouse L cells transfected with the gene for the human cellular receptor for poliovirus), demonstrates selectivity specifically for Poliovirus. On the other hand, the RD cell line (Human Rhabdomyosarcoma) exhibits a broader selectivity towards Enteroviruses, including Poliovirus **[13]**. Following the observation of samples for cytopathic effects (CPE) using the L20B cell line, further differentiation between various serotypes of polioviruses can be achieved using the real-time polymerase chain reaction (RT-PCR) technique.

7. Intestinal response to oral polio vaccine

For many years, live attenuated poliovirus vaccines have played a crucial role in vaccination programs and remain indispensable in the global efforts to eradicate the wild-type virus. Upon administration, the vaccine undergoes replication within recipients for an average duration of four weeks. Throughout this period, the properties of the excreted virus go through alterations **[14]**. On the other hand, the Salk-inactivated polio vaccine (IPV) has limited influence on viral replication in the gastrointestinal tract when faced with OPV vaccine challenge in individuals who have never

encountered a live virus. Nevertheless, IPV generates substantial systemic immunity and offers protection against paralysis-related illnesses **[15]**. Various investigations into mucosal antibody responses following the administration of combined bivalent oral polio vaccine (bOPV) and inactivated polio vaccine (IPV) regimens have consistently emphasized the vital role of IgA-mediated neutralizing antibody responses in limiting poliovirus replication in the gastrointestinal tract. However, attempts to enhance serum neutralization by incorporating standard or high-dose IPV into the primary bOPV immunization series do not yield a comparable increase in intestinal immunity when subsequently exposed to live type-2 poliovirus. This underscores the distinct nature of polio-specific intestinal immunity, which differs from the serum response and plays a critical role in viral excretion **[16-17]**.

8. Vaccine-associated paralytic poliomyelitis and Vaccine Derived Poliovirus

One of the major aspects of OPV is its ability to spread to unvaccinated groups of individuals through coming into contact with vaccinated populations, which results in widespread protection against poliomyelitis **[18]**. Despite the tremendous and life-saving benefits of OPV, it has certain drawbacks. One of them is the occurrence of Vaccine-associated paralytic poliomyelitis (VAPP), which is a rare but serious adverse event linked to the administration of oral polio vaccine (OPV). Onset typically manifests within a timeframe of 60 days following OPV exposure, although it can occur, less frequently, after receiving the inactivated polio vaccine (IPV) **[19]**. VAPP typically occurs in individuals who have received the oral polio vaccine, but it can also occur in close contact with vaccinated individuals who are exposed to the virus shed in the stool. The risk of VAPP is highest in the first few weeks after vaccination but remains extremely low. The incidence of VAPP has been estimated to be around one case per 2.4 million doses of OPV administered **[20]**.

9. Poliovirus Categorizing

First, OPV-like isolates (Sabin-like), isolates have minimal genetic variations, less than 1% in the VP1 nucleotide sequence, compared to the original Sabin strains used in the oral polio vaccine (OPV). Second, VDPVs exhibit genetic differences ranging from 1% to 15% in the VP1 nucleotide sequence compared to the parental Sabin strains. This corresponds to at least 10 nucleotide substitutions. VDPVs can emerge in individuals or communities with low immunity and have the potential to cause polio-like infections. Third, wild polioviruses are found in the environment of AFP cases and are responsible for cases of natural polio infection. They differ from the Sabin strains by more than 15% of VP1 nucleotides, indicating significant genetic divergence **[21]**.

Within the VDPV category, there are subcategories, depending on the sampling source and epidemiologic data including: i). Immunodeficiency-associated VDPVs (iVDPVs) were isolated from individuals with immunodeficiency who experience prolonged infections following exposure to the oral polio vaccine; ii) Circulating VDPVs (cVDPVs) are distinguished by continuous person-to-person transmission. They are associated with continuous transmission within a community or population; iii). Ambiguous VDPVs (aVDPVs) are clinical isolates isolated from patients who do not have a known immunodeficiency and are not associated with any specific epidemic. They may also contain environmental isolates whose origin or source has not yet been determined. It is vital to highlight that these classifications aid in understanding the features and transmission patterns of vaccine-derived polioviruses, which is critical for monitoring and implementing

effective public health measures to prevent the spread of polio **[21]**. Also, in this review, we highlight that VAPP is a clinical disease, while VDPVs are viruses with unique genetic characteristics. VAPP cases show a temporal relationship between OPV exposure and paralysis onset. VDPV isolates have more genetic divergence from OPV strains than isolates from most VAPP cases, suggesting a unique clinical or epidemiologic background for VDPVs.

9.1. Immunodeficiency-associated vaccine-derived polioviruses (iVDPVs)

Primary antibody deficiencies are the most prevalent group of primary immunodeficiencies. Several molecular defects have been identified in the pathways responsible for B-cell development **[22]**. The only treatment for this category is treatment with intravenous immunoglobulin. Individuals with primary B-cell immunodeficiencies can experience chronic infection, genetic changes, and shedding of vaccine-derived polioviruses known as immunodeficiency-associated VDPVs (iVDPVs) following exposure to oral polio vaccine (OPV) **[23]**. The case will acquire AFP symptoms, which after lab analysis will establish the presence of VDPV. Over time, the viral genome acquires an increasing number of nucleotide mutations, leading to neurovirulence. Although exceedingly rare, certain immunodeficient persons can excrete VDPVs for extended periods (>6 months), creating a risk of infection in the population **[2]**. Some patients' iVDPVs could even replicate and excrete for months or years **[24-25]**. On the other hand, Wang et al. (2017) reported one case in China excreted VDPVs for 20 months and another case reported in the United Kingdom excreted VDPV for about 30 years without any paralytic symptoms **[26-27]**.

9.2. Circulating Vaccine-derived poliovirus (cVDPVs)

In recent years, there has been a notable shift in the risk associated with OPV exposure. In many parts of the world, population immunity against poliovirus relies primarily on immunization. However, when polio vaccine coverage rates decline while OPV usage continues, circumstances may arise that increase the chances of person-to-person transmission of vaccine-derived polioviruses (VDPVs). The duration and extent of such transmission depend on the magnitude of the immunity gap and the intensity of other risk factors that facilitate the circulation of polioviruses such as low vaccination coverage, poor sanitation and hygiene, immunosuppression, and finally Population movement and travel. This previously discussed theoretical concern has become a reality with the occurrence of outbreaks of paralytic polio linked to the circulation of circulating VDPVs (cVDPVs) **[28]**. The primary distinguishing characteristics of cVDPV isolates are their heightened ability to cause paralysis in individuals and their sustained person-to-person transmission capability.

Experimental testing has revealed that cVDPV isolates exhibit neurovirulence levels equivalent to those of wild polioviruses in transgenic mice expressing the human receptor for poliovirus. Similar to wild polioviruses, cVDPV isolates demonstrate the capacity to replicate to high titers in cell culture at temperatures above optimal conditions. Furthermore, all characterized cVDPV isolates exhibit antigenic properties that more closely resemble those of wild polioviruses rather than the original Sabin strains **[29]**. The primary and critical risk factor for cVDPV outbreaks, similar to wild poliovirus outbreaks, is inadequate population immunity. This risk is further influenced by various factors that facilitate the circulation of poliovirus, including the number and density of individuals susceptible to

infection, the birth rate, deficiencies in hygiene and sanitation practices, and the duration of tropical conditions during specific seasons **[30]**.

9.3. Ambiguous vaccine-derived poliovirus (aVDPVs)

These are strains isolated from people with or without AFP who are not immune-compromised, or from environmental samples that show no signs of circulation. The advent of ambiguous vaccine-derived poliovirus (aVDPV) presents a substantial challenge to global efforts to eradicate polio. aVDPVs are poliovirus strains that have mutated from the attenuated strain seen in the oral polio vaccination (OPV) **[31]**. While OPV has played an important role in reducing the prevalence of wild poliovirus, in rare situations, the weakened virus in the vaccine might regain potency and cause polio infections. aVDPVs, like wild poliovirus, can spread throughout populations and create outbreaks. This uncertainty arises because, whereas OPV protects against wild poliovirus, it can also lead to the formation of aVDPV. **Table 1** shows different VDPVs that recently took place over the world (2019-2022).

Table 1. Vaccine-derived poliovirus (VDPVs) all over the world (2019-2022)

Type of VDPV	Source	Percent Divergence	Year of collection	Reference	Country
cVDPV2	AFP case	-	2022	**[32]**	Indonesia
WPV1	AFP Case	-	2022	**[33]**	Pakistan
cVDPV-2	Sewage	1.9%	2020	**[34]**	East Region in Cameron
cVDPV-2	Sewage	2%	2019	**[34]**	Far North Region in Cameron
*VDPV-1	Sewage	3.5%	2019	**[35]**	Malaysia
cVDPV-1	AFP case	3.8%	2019	**[35]**	Philippines
cVDPV-2	Sewage	6.8–7.2%	2019	**[35]**	Malaysia
iVDPV-2	PID case	7.1%	2019	**[35]**	Philippines
VDPV2	Contacts	-	2014	**[36]**	Uganda

*cVDPV1 (The first reported one) in Malaysia with genetic linkage to the cVDPV1 isolated from the AFP case in the Philippines.

Since the beginning of 2021, all instances of wild poliovirus type 1 (WPV1) infections in Pakistan have been concentrated in seven polio-endemic regions within the southern province of Khyber Pakhtunkhwa, despite there being 171 districts nationwide. These areas specifically target approximately 1.1 million children under the age of five. The success of polio eradication efforts in the country hinges on effectively targeting these districts and ensuring comprehensive vaccination coverage among the remaining under-vaccinated and unvaccinated children. The proportion of WPV1-positive environmental samples in Pakistan decreased from 8% in 2021 to 4% in 2022. However, the periodic detection of WPV1 in sewage water

samples from areas beyond the southern region of Khyber Pakhtunkhwa highlights the ongoing risk of transmission. Nevertheless, the geographical extent of endemic WPV1 cases during the year 2022 was more limited compared to previous periods, indicating progress in containment efforts **[32]**.

In establishing a collaborative epidemiological partnership between Pakistan and Afghanistan, a comprehensive analysis of the situation in Afghanistan revealed highly encouraging results. Despite the political transformations that unfolded in the country in 2021, there was notable progress in terms of improved access to healthcare services for all children, including over 3.5 million children who had remained unreached for nearly five years. This improvement extended to enhanced vaccination coverage and disease surveillance, which significantly fortified the polio eradication program in Afghanistan. However, these achievements occurred within the context of a distressing backdrop marked by a severe and acute humanitarian crisis as well as political instability **[33]**.

During the latter half of 2022, an extensive Outbreak Response Assessment was conducted in southeast Africa to evaluate the regional response to the simultaneous outbreaks of wild poliovirus type 1 (WPV1) and circulating vaccine-derived poliovirus (cVDPV). The WPV1 outbreak in the region was traced back to the virus originating from Pakistan, with confirmed cases reported in Malawi and Mozambique. Additionally, multiple cVDPV outbreaks were identified. Notably, experts participating in the assessment acknowledged the remarkable level of comprehensive support and supervision dedicated to managing the outbreaks throughout the region, despite the presence of competing and intricate priorities **[37]**.

In November, the Nigerian Government, in collaboration with partners from the GPEI, hosted the Global Roundtable Discussion on outbreaks of circulating vaccine-derived poliovirus type 2 (cVDPV2). The purpose of the meeting was to assess the progress made in response to the surge in cVDPV2 cases observed in 2021. During the discussion, participants acknowledged the concerted efforts undertaken to reach children who had not received any doses of the polio vaccine, particularly in the consequential regions across Nigeria. Notably, the novel oral polio vaccine type 2 (nOPV2) played a significant role in these efforts. The country also emphasized the importance of strengthening routine immunization through the use of bivalent oral polio vaccine and inactivated polio vaccine. However, the group emphasized that regardless of the chosen strategy, achieving high coverage rates is paramount. They highlighted that the effectiveness of any vaccine is contingent upon the proportion of children who receive it **[32, 38]**.

In addition to the aforementioned points, it is worth noting the significant impact of vaccine-derived poliovirus (VDPV) in Egypt, as documented by the World Health Organization's polio database **[39]**. The data revealed that by the end of 2021, Egypt had experienced a staggering 79 cases of vaccine-derived poliovirus. This outbreak prompted the WHO to initiate an urgent vaccination campaign in the country, utilizing the newly developed genetically modified nOPV-2 poliovirus vaccine. The campaign, which concluded successfully in December 2021 **[40]**, marked a milestone for Egypt as it became the first country in the Eastern Mediterranean Region (EMRO) to employ the nOPV2 vaccine. This proactive approach highlights the commitment of Egypt and the WHO to combat the spread of vaccine-derived poliovirus and protect public health.

Regrettably, the efficacy of the new vaccine

in addressing the VDPV-detected cases in Egypt was not as significant as anticipated. By the end of 2022, Egypt had identified an additional six isolates of VDPV-2, despite the implementation of the vaccination campaign **(Table 2)**. These findings indicate the ongoing challenges and complexities associated with controlling and eliminating VDPV. It underscores the need for continuous surveillance, research, and development of more effective interventions to address the persistence of VDPV and ensure the success of global polio eradication efforts **[41]**.

Table 2. Number of the obtained isolates in the EMRO region during 2021/2022 [32]

	AFG		DIJ		PAK		EGY		IRN		IRQ		JOR		KUW		LEB		SOM		SUD		SYR		YEM	
Year 2020/2021	**2020**	**2021**	**2020**	**2021**	**2020**	**2021**	**2020**	**2021**	**2020**	**2021**	**2021**	**2020**	**2021**	**2020**	**2021**	**2020**	**2021**	**2020**	**2021**	**2020**	**2021**	**2020**	**2021**	**2020**	**2021**
Wild		20			45	37																				
cVDPV2	39		5	12	19		12	6	1										1	3		1			13	10
Wild+cVDPV2	1				16																					
Wild+aVDPV2					4																					
Wild+aVDPV3																										
aVDPV1																										
aVDPV2	3				33	1			2																	
aVDPV3																										
VDPV1					1		1																			
VDPV2							67	1		1				3						1						1
SL2	145	68		1	266	16	192		9	4									2	15	4					
SL1/3	44	149	2		151	386	168	235	16	23	2	18	20				9	23	10	2	1	2	28	26	1	
Entero	235	406	6	9	314	644	265	284	42	36	58	14	29	7	2	36	24	60	37	53	79	162	140	1		
Negative	12	21	13		9	17	26			1	4		22	16	17	5	13	67	90	41	57	14	17			

AFG, Afghanistan; DJJ, DJIBOUTI; PKA, Pakistan; IRN, Iran; IRQ, Iraq; JOR, Jordon; KUW, Kuwait; LEB, Lebanon; SOM, Somalia; SUD, Sudan; SYR, Syria; YEM Yemen.

10. Global response to outbreaks

The cornerstone for any outbreak will be the EPI (Extended Program of Immunization), MOH, WHO, and GPEI. GPEI provides technical support and financial assistance to countries in their efforts to respond to poliovirus incidents or outbreaks **[38]**. Response actions consist of two important elements: i) conducting at least two high-quality supplemental immunization activities (SIAs) that target children under 5 years old (or older, depending on epidemiology); and ii) enhancing surveillance sensitivity to detect poliovirus. In the event of cross-border outbreaks, countries are advised to coordinate synchronized SIAs and implement additional measures to improve surveillance. It is not recommended to administer monovalent OPV type 2 (mOPV2) and bivalent OPV (bOPV) sequentially or concurrently when there are co-circulating outbreaks of cVDPV types 1/2 or 2/3.

Future Perspectives

The development and approval of Novel Oral polio vaccine type 2 (nOPV2), the first vaccine targeting type 2 poliovirus, marked a significant milestone. It was also the first vaccine to receive authorization from the WHO Prequalification team through its Emergency Use Listing procedure. As a result, around 450 million doses of nOPV2 have been distributed across 21 countries to effectively manage outbreaks **[39]**. To address the sporadic occurrence of illnesses and outbreaks associated with the genetic instability of the Sabin vaccine strains, researchers are working on the development of new oral poliovirus vaccine type 2 (nOPV2) candidates. One of these novel vaccine strain candidates features a genetically stabilized domain V called "S15."

The strategy of thermodynamically strengthening the RNA structure through point mutations was limited, as it does not involve U-G base pairs. However, it effectively maintains the attenuation of virulence at a level comparable to that of the Sabin strains, while significantly reducing the risk of virulence reversion caused by single-nucleotide changes **[40]**. Subsequently, another innovative oral poliovirus vaccine type 2 candidate (nOPV2-c1) was developed with two additional modifications to minimize the risk of reversion in the "S15" domain V due to a single recombination event. Firstly, the cis-acting replication element (cre) was relocated to the 5' untranslated region (5UTR) of the viral genome. Secondly, two alterations were made to the 3D polymerase, reducing the occurrence of recombination events and enhancing replication fidelity. In parallel, a distinct oral poliovirus vaccine type 2 candidate (nOPV2-c2) supplements the S15 domain V with codon deoptimization in the capsid region as an additional measure to further attenuate the strain **[41]**.

Conclusion

The international dissemination of poliovirus has been designated as a Public Health Emergency of International Concern (PHEIC) by the International Health Regulations (IHR) 2005, pertaining to both wild poliovirus type 1 (WPV1) and circulating vaccine-derived poliovirus (cVDPV). The IHR's emergency committee determined an escalating risk of cVDPV2 transmission, based on the increase in reported cases, identification of viral material in the environment, and documented cross-border incidents. This risk was further exacerbated by the declining level of intestinal mucosal immunity against poliovirus type 2 since the discontinuation of trivalent oral polio vaccine (tOPV) usage in 2016. Global response actions to contain the spread and occurrence of poliomyelitis consist of conducting at least two high-quality supplemental immunization activities targeting children under 5 years old or older and enhancing surveillance sensitivity to detect poliovirus. Researchers are working on the development of novel oral poliovirus vaccines of type 2 through genetically stabilizing the domain V reducing the occurrence of recombination events and enhancing the replication fidelity of the viral RNA genome.

Declarations

Consent to publish

All authors have read and agreed to the published version of the manuscript

Ethics approval and consent to participate

Not applicable.

Availability of data and material

All data generated or analyzed during this study are included in this published article in the main manuscript.

Conflict of Interest

The authors assert that there are no conflicts of interest.

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Authors Contribution

All authors contributed to the study's conception and design. The first draft of the manuscript was written by MAR. Revised by NSE and KMA. All authors read and approved the final manuscript.

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Author Disclosure Statement

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