MODELLING THE TIME-VARYING TRANSMISSION OF WILD POLIOVIRUS IN PAKISTAN

Abstract

The efforts to eradicate the wild poliovirus since 1988 have successfully reduced its global prevalence by 99%. However, as of 2023, Pakistan and Afghanistan remain the only two endemic countries facing continual virus transmission. In this study, an ordinary differential equations-based deterministic model was developed to assess the persistence of wild poliovirus type 1 (WPV1) in Pakistan. The model considered both human-human and environment-human virus transmission represented by time-dependent transmission rates. The model was calibrated by fitting the reported data of WPV1 cases from 2017 to 2022 in Pakistan. The model showed a better predictive ability than the usual constant transmission rate models. The results suggest that endemic virus transmission will continue in Pakistan subject to the current higher vaccination rates. The numerical simulations considering the reduction in the virus-shedding rate by the asymptomatic infectious population through targeted vaccinations indicated a reduction in the number of future cases in Pakistan. The model can be further utilized to guide eradication efforts for the targeted allocation of preemptive measures through the incorporation of spatial data of routine surveillance and vaccination coverage in the country.

Keywords: Dynamic modeling, polio eradication, transmission ecology, risk analysis, biomathematics, vaccination, environmental surveillance

Introduction

Poliomyelitis (Polio) is a highly contagious, potentially debilitating, and incurable disease caused by the poliovirus. The virus primarily affects children under the age of five years and can invade the central nervous system, resulting in permanent paralysis (Walter and Malani 2022). Transmission occurs through either the fecal-oral or oral-oral route (Chen et al. 2021). In the early 20th century, polio was the most feared pathogen in industrialized nations until the development of a vaccine in the 1950s (Jubelt and Lipton 2014). Since the launch of the Global Polio Eradication Initiative (GPEI) by the World Health Organization (WHO) in 1988, wild poliovirus infections worldwide have reduced significantly. Mass immunization against the virus has led to the complete eradication of wild poliovirus serotypes 2 and 3, leaving only two endemic countries, Pakistan and Afghanistan, still affected by wild poliovirus type 1 (WPV1) transmission (Falleiros-Arlant et al. 2020; Lee et al. 2023). This ongoing circulation of the virus not only poses a threat to the health of residents in these countries but also hinders vaccination efforts in polio-free regions (Rana et al. 2022).

Intensified immunization efforts have reduced the incidence of wild poliovirus cases in Pakistan; however, the country faces several challenges in effectively implementing eradication policies. These challenges include geopolitical instability, government negligence, lack of efficient public health infrastructure, and general misconceptions regarding polio vaccines (Shabbir et al. 2022). Moreover, the neighboring country; Afghanistan is also battling constant virus transmission which poses an immense threat to eradication efforts in Pakistan as the two countries are considered to be one epidemiological block due to the highly porous border and extensive population migrations (Roberts Leslie 2018). Thus, it has been considered that if Pakistan achieves eradication Afghanistan will soon follow and the world will eventually achieve a milestone of global polio eradication.

Mathematical models have long assisted policymakers in identifying improved vaccination strategies and optimizing surveillance (Thompson and Kalkowska 2020). In this study, we developed a deterministic mathematical model based on ordinary differential equations (ODEs) to evaluate poliovirus transmission in Pakistan. This model considers both human-human and environment-human transmission of the virus through the fecal-oral route owing to sewage water contamination, which facilitates its spread (Hovi et al. 2001). This route is also the focus of environmental surveillance efforts to eradicate wild poliovirus from the remaining endemic countries. Another significant aspect of this study is the incorporation of

different types of time-dependent transmission rates to reflect the epidemiological characteristics of polio infections in the country. These transmission rates change in response to various intervention measures and human behavior during different periods. By incorporating these features, our model can improve its predictive accuracy and enhance our understanding of the periodic outbreaks of the virus in Pakistan. Thus it will lead to an effective resource allocation to interrupt the transmission and achieve eradication.

Methods

A mathematical model was adapted to understand the transmission dynamics of WPV1 in Pakistan. Our modelling strategy is inspired by the approach used by Yang and Wang (2021) to model COVID-19 transmission in Hamilton County, Tennessee, United States. In our model, the target population is divided into four classes: susceptible individuals 'S', exposed individuals 'E', reported wild poliovirus cases 'I', and recovered individuals 'R', while compartment 'W' represents the poliovirus in sewage water. The original model divided the host population into five classes, including hospitalized individuals, with the sixth compartment representing the concentration of coronavirus aerosols in the environment. Furthermore, the model assumed that the entire target population was susceptible to COVID-19, as the vaccine had not yet been introduced. Therefore, because the entire target population is susceptible, no scaling of the disease data is necessary. In contrast, our model includes children up to the age of five who did not receive OPV during the annual National Immunization Days (NIDs) from 2017-2022 as the susceptible population. **Figure 2** shows the NIDs conducted in Pakistan during this period along with the percentage of children who were still missed by these campaigns. The 'E' compartment represents the number of asymptomatic infections. We assumed that 70% of poliovirus infections would be asymptomatic (Walter and Malani 2022). The total number of WPV1 cases reported in the country during the targeted years is shown in **Figure 1**. Data scaling was performed to provide the model with a more balanced landscape for training, leading to an improved efficiency and predictive ability.

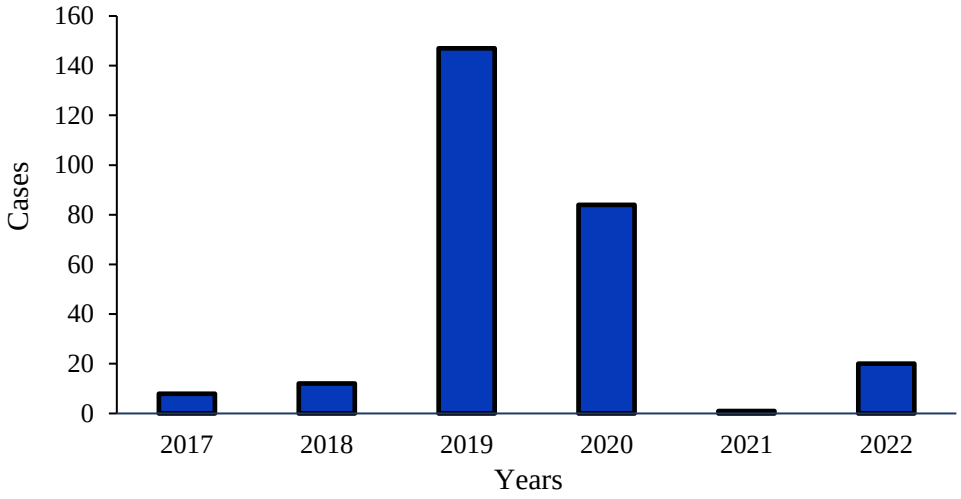

Fig 1. Reported WPV1 cases in Pakistan from 2017-2022.

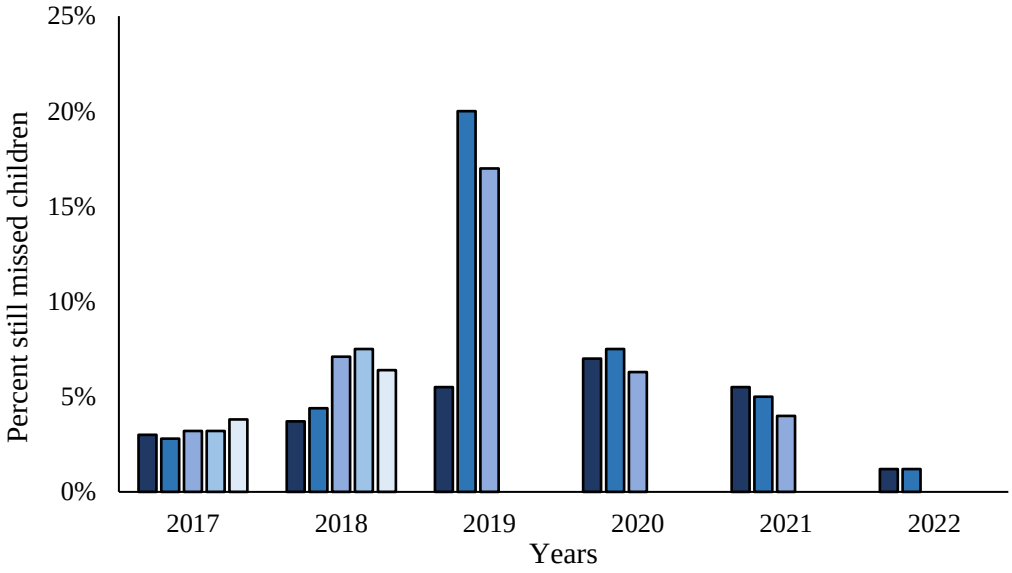

Fig 2. National Immunization Activities occurred from 2017-2022 in Pakistan. The number of columns are representing the number of campaigns of every year and their height is indicating the proportion of missed children by each campaign (Elhamidi et al. 2017; Hsu et al. 2018; Moffett et al. 2019; Chard et al. 2020; Mbaeyi et al. 2021)

The following set of ordinary differential equations represents our model:

$$\frac{dS}{dt} = \Lambda - \beta_E (I, t)\, SE - \beta_I (I, t)\, SI - \beta_W (I, t)\, SW - \mu S$$

$$\frac{dE}{dt} = \beta_E (I, t)\, SE + \beta_I (I, t)\, SI + \beta_W (I, t)\, SW - (\alpha + \gamma_1 + \mu)\, E$$

$$\frac{dI}{dt} = \alpha (1-p)\, E - (q + \gamma_2 + \mu)\, I$$

$$\frac{dR}{dt} = \gamma_1 E + \gamma_2 I - \mu R$$

$$\frac{dW}{dt} = \xi_1 E + \xi_2 I - \sigma W$$

Where the 'Λ' is a parameter for population inflow, μ = death rate, α = average incubation period of poliovirus, 'p' represents the proportion of asymptomatic population who develop paralysis, q = rate of infected persons who develop paralysis, σ is the removal rate of poliovirus from the environment; γ_1 and γ_2 are the rates of recovery of asymptomatic and symptomatic persons and ξ_1 and ξ_2 are the rates of contributing virus to the environment by the exposed and infected population respectively. These parameter values were obtained from a literature search and are listed in **Table 1**. The schematic representation of the model is given in **Figure 3**.

Table 1. Model parameter values for poliomyelitis

Parameters	**Values**	**References**
Incubation period(α)	12 days	(Estivariz et al. 2021)
Population size(N)	40000000	(Mbaeyi et al. 2021)
Natural Birth & Death rate(μ)	160	(UNICEF 2023)
Environmental Removal Rate of virus(σ)	0.12/d	(Bae and Schwab 2008)
Virus shedding rate by infected persons(ξ2)	0.025/ml/person/day	(Lodder et al. 2012)
Virus shedding rate by exposed persons(ξ1)	0.45/ml/person/day	(Mach et al. 2014)
Recovery rate of exposed individuals(γ1)	1/10/d	(Estivariz et al. 2021)
Recovery rate of infected individuals(γ2)	1/14/d	(Ben-Joseph 2022)
Rate of paralysis in exposed individuals(p)	1.5%	(Mehndiratta et al. 2014)
Rate of paralysis in infected individuals(q)	<1%	(Mehndiratta et al. 2014)

The incubation period of the poliovirus was considered to range from 3-21 days, in this study, the average value of 1/α = 12 days was considered (Estivariz et al. 2021). The recovery period from polio depends on different factors, including the severity and immune status of infected children. The model includes the recovery period of the exposed and infected children. In cases of recovery from an asymptomatic state, the population usually shows no symptoms. The time period for this recovery was considered to be 7-14 days and in this model, an average recovery period of 10 days was considered for those 70% of infections that go unnoticed, which gives γ_1 = 1/10 per day (Estivariz et al. 2021). Because it is a paralytic disease, in such cases, there is no recovery, but rather a permanent disability or death. However, those who experience milder symptoms can recover within 1-2 weeks, so a complete recovery period of 14 days was considered, which gives γ_1 = 1/14 per day (Ben-Joseph 2022). Evaluation of the poliovirus removal rate from the environment showed a time period of 3 hours which led to 90% removal

of the virus from the environment. Therefore, the virus removal rate from the environment was taken as $\sigma = 0.12$ per day (Bae and Schwab 2008). Population immigration and emigration rates across the country were considered equivalent; thus, the rate of influx of the at-risk population was $\Lambda = \mu N$, where N is the magnitude of the target population. Due to the small target population, the natural birth and death rates of the population were considered equal to μ (Yang and Wang 2021). The shedding rate of wild poliovirus by the asymptomatic population (Mach et al. 2014) and infected individuals (Lodder et al. 2012) was taken from the literature. The rate of paralysis in asymptomatic infections was $p = 1.5\%$ and that in in infected individuals was $q = 1\%$ (Mehndiratta et al. 2014)

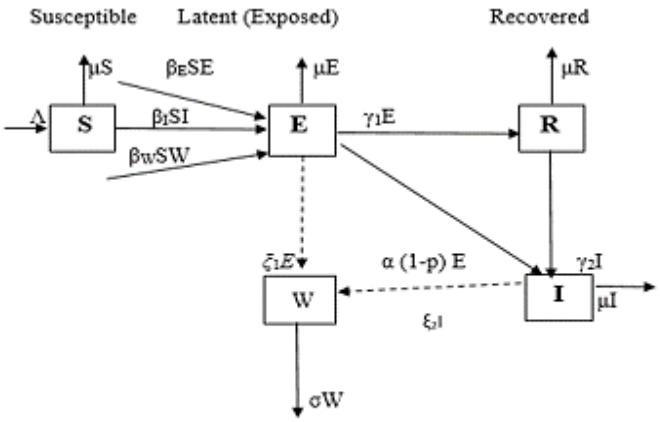

Figure 3. An SEIRW model adapted for poliovirus transmission in Pakistan incorporating the effect of virus contaminated environment on the spread of the disease.

The model incorporated multiple transmission routes and each of which was associated with non-linear incidence. The functions $\beta_E(I, t)$ and $\beta_I(I, t)$ indicate the direct, human-human transmission rates between asymptomatic and susceptible populations and between infected and susceptible populations, respectively. The $\beta_W(I, t)$ function depicts the environment-human transmission rate. The model considered the chance of the infected (both latent and clinical) population coming into contact with other individuals and which could lead to shedding of the poliovirus into the environment by those individuals. Our assumption is based on the fact that in densely populated areas with poor sanitation facilities and an under-immunized or zero-dose population, the presence of poliovirus in the environment can pose a significant threat to the susceptible population (Mach et al. 2017). The values of the transmission rate parameters were obtained by fitting model to reported data. The considered time domain was divided into two 3-year time periods. These have distinct time intervals: $[T_1, T_2]$ and $[T_2, T]$ and for some

positive constants, $T_1 < T_2 < T$. The first period from 2017 to 2019 was considered the period of increased vaccine resistance **Figure 2**, which eventually led to a surge in polio cases in Pakistan in 2019. We assumed that the disease transmission rate increased monotonically during the first period. The second time period from 2020-2022, on the other hand, was a period of increment in vaccination rates **Figure 2** and reduced exposure of the susceptible population to infectious individuals due to the nationwide lockdown to contain the COVID-19 pandemic. Thus, the transmission saw a major decline during this period and was assumed to no longer increase monotonically. The separate transmission rates for each of these periods were then developed to represent their unique properties.

- **Period 1**: Here, we considered that all the transmission rates were increasing with the time 't' during this transitional interval and are described as

  $\beta_E(I, t) = \beta_{E0} f(t)$, $\beta_I(I, t) = \beta_{I0} f(t)$, $\beta_W(I, t) = \beta_{W0} f(t)$

  $f(t) = 1+d(t-T_1)$ with $T_1 \leq t \leq T_2$.

  Each transmission rate initiates from the minimum $t = T_1$ and grows monotonically relative to t with a constant rate d. Parameter d was estimated through model fitting to the disease data.

- **Period 2**: In this period, the transmission rates no longer increase monotonically but take the form

  $\beta_E(I, t) = \beta_{E0} f(T_2) g(I)$, $\beta_I(I, t) = \beta_{I0} f(T_2) g(I)$, $\beta_W(I, t) = \beta_{W0} f(T_2) g(I)$,

  Here, $f(t) = 1+d(T_2-T_1)$, and $g(I) = 1 - \frac{2}{\pi}\tan^{-1}(c\cdot (I(t) - I(T_2)))$

Where $T_2 < t < T$ and function g(I) represents the variation in transmission rates in relation to I. This variation was due to increased vaccination and reduced exposure rates. The infection prevalence at the beginning of this period, $t = T_2$, was represented by $I(T_2)$. The constant 'c' is used to adjust the magnitude of the difference, and its value is determined through data fitting. In addition, an inverse tangent was used to transfer this difference to a standard interval.

Our modelling strategy considers the time-dependent transmission rates of wild poliovirus in Pakistan. Typically, infectious disease models for poliovirus transmission in one of the last reservoirs of the virus consider only constant transmission scenario. By considering time-dependent transmission rates, we can enhance the accuracy of model predictions for future

disease trajectories in the country. This will also help us develop effective intervention strategies to control viral transmission.

Results

A SEIRW model was developed to study the transmission and spread of WPV1 in Pakistan. The disease pattern was observed during two periods: pre-COVID-19 (2017-2019) and COVID-19 (2020-2022). In the pre-COVID-19 era, there was a rapid increase in the number of new cases, which can be attributed to a reduction in vaccination rates (Figure 1 & 2). However, in the COVID era, the number of cases decreased owing to increased vaccination rates and reduced exposure rates resulting from stay-at-home orders implemented to contain the transmission of COVID-19. Transmission rates were formulated for each of these periods, as previously described, to conduct data fitting and model simulations.

Model fitting to WPV1 cases in Pakistan during pre-COVID period (2017-2019)

Initially data fitting was conducted for the pre-COVID era from 2017 to 2019 to estimate the values of the three transmission parameters, with two parameters representing human-human transmission and the other representing environment-human transmission. Based on the demographic and reported data, the initial conditions for this time period were set as (S, E, I, R, W) = (1200000, 0.12, 0.05, 0, 22). The value of poliovirus concentration in the sewage water was obtained as 22 virions/ml (Hovi et al. 2001). Because our model did not consider developed immunity, the recovered individuals were considered to be equal to zero as an initial value for model calibration **Figure 4**. Data fitting was performed using the estimated parameter values listed in **Table 2**.

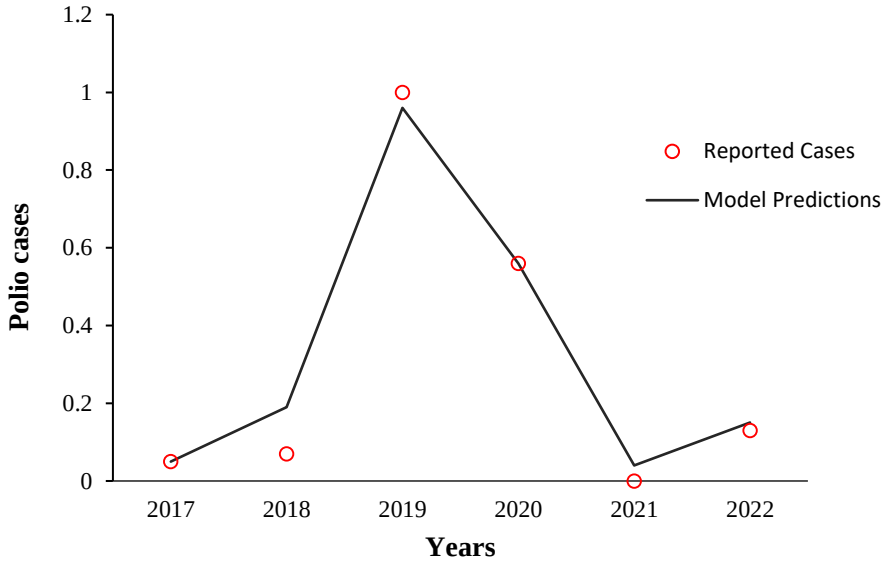

Figure 4. Model fitting results for the reported cases of Polio in Pakistan from 2017-2022.

These results confirmed our assumption that a decrease in vaccination rates led to an increased transmission rate. The estimated parameter values clearly showed that asymptomatic individuals pose a significant threat to susceptible individuals. Parameter d represents the rate of transmission increment during this time period as a function of t, and its estimated value is presented in **Table 3**. This increase was consistent and steadily rising, so instead of a decline in the epidemic curve, we observed a sharp surge in virus transmission and an increase in cases.

Table 2. WPV1 model parameter values estimated through model calibration.

Estimated parameters		**Values**
	Transmission rate from asymptomatic to susceptible population (β_E)	$3x10^{-6}\ person^{-1}year^{-1}$
	Transmission rate from infected to susceptible population (β_I)	$2x10^{-6}person^{-1}year^{-1}$

Environment -Human transmission rate	Transmission rate from environment to susceptible population (β_C)	$1.5x10^{-6} person^{-1} year^{-1}$

During this period, the transmission of the system was not autonomous because it depended on the time. In mathematical terms, a system of ordinary differential equations that relies on time as its independent variable is referred to as a non-autonomous system. The rate of transmission, represented by the parameter 'd', increased over time, denoted by 't'. Because we assume that the increase in transmission during this period was due to a decrease in vaccination rates, the system can be classified as non-autonomous. Consequently, the basic reproduction number (R0) for a specific time domain was not calculated. In situations where there is no delay between exposure and appearance of clinical cases, the reproduction number can be calculated by excluding the latent infection period. However, this approach cannot be applied to polio infections.

Model fitting to WPV1 cases in Pakistan during COVID pandemic (2020-2022)

During the period 2020-2022, there was a more stable spread of infection as transmission no longer increasing monotonically. This was a result of higher vaccination rates and decreased exposure of vulnerable populations to infectious individuals due to stay-at-home orders issued during the COVID-19 pandemic. The data fitting results are shown in **Figure 4** and **Table 3** displays the estimated value of parameter c for this specific time frame. This parameter was used to add an extra dimension and transform the previous system of non-autonomous ODEs into an autonomous system. As a result, the transmission rates of poliovirus during this period were no longer dependent on time, but instead on the prevalence of polio infections in the population. The system was assumed to be time independent. Transmission now varies based on the contact rates between susceptible and infectious populations, as well as the number of individuals in both groups. Model calibration during this time period revealed that transmission was significantly reduced due to a decrease in contacts and the number of at-risk individuals as immunization rates increased.

Table 3. WPV1 model Parameter values estimated through model calibrations

Rate of increase in transmission rate during the period of 2017-2019 **(d)** (Period 1)	0.385/year
Adjustment Parameter **(c)** (Period 2)	0.4/person

Here, in-sample validation was used for the re-substitution validation method, where the goodness of fit was measured and compared using the root mean square error (RMSE) for our assumption of time-dependent transmission rates while for the model of COVID-19 transmission, normalized root mean square error (NRMSE) was used (Yang and Wang 2021). The formula for RMSE has been given as

$$\text{RMSE} = \sqrt{\frac{\sum_{i=1}^{N}(\text{Predicted}_i - \text{Actual}_i)^2}{N}}$$

The 'N' represents the number of total data points in the data set. The RMSE value was 0.05, indicating good model accuracy and validating our assumption of time-dependent transmission rates compared with other models that consider constant transmission scenarios. Yang and Wang, (2021) also tested the validity of the constant transmission rate scenario for COVID-19 transmission and found it to be less accurate than the assumption of a time-dependent transmission rate. On the other hand, we did not consider the model fitting results for the constant transmission rate for the entire period of 2017-2022. However, upon testing the validity of this assumption using the RMSE, the obtained value was 0.44. This makes the constant transmission rate scenario less fitting than the the time-dependent transmission rates for the two time periods.

Reproduction number (R_0)

The basic reproduction number (R_0) is the average number of secondary infections caused by an initially infected person over their lifetime, when the entire population is susceptible. If $R_0 \leq 1$, the pathogen will be cleared from the population. However, if $R_0 > 1$, the pathogen can spread throughout a susceptible population. R_0 is a crucial parameter for estimating the ability of a pathogen to spread and cause an outbreak. This provides valuable insights into the efforts required to control the disease, such as prompt case identification, quarantine measures, and physical distancing to prevent contact between susceptible and infected individuals.

In our developed model, the first time period is a non-autonomous time-dependent system, making it challenging to define the reproduction number for this period. The argument here is that non-autonomous disease dynamic systems consider the periodicity of infection occurrences. Therefore, the reproduction number becomes a function of time which can be calculated either by disregarding the recruitment of susceptible individuals in the model, or by overlooking the latent stage of infection.

However, the reproduction numbers of time-averaged systems (autonomous systems) are sufficient to explain the mitigation policies that need to be implemented. Thus, in the second instance, our model is an autonomous dynamic system in which the rate of disease transmission is solely a function of prevalence (I). The reproduction number (R_0) for this period can be calculated as follows.

$\beta_E(I, t) = \beta_E(I)$, $\beta_I(I, t) = \beta_I(I)$ and $\beta_W(I, t) = \beta_W(I)$ for $T_2 \leq t \leq T$.

Here, the standard method for calculating the basic reproduction number, which is the next-generation matrix technique was used

Apparently, the ODE system of equations has a condition for the absence of the disease referred to as the disease-free equilibrium (DFE) at

$X_0 = (S_0, E_0, I_0, R_0, W_0) = (\frac{\Lambda}{\mu}, 0, 0, 0, 0)$

Here, E, I and W are considered as the infectious elements. Matrices F and V represent new infections and transitions between different disease stages, respectively.

$$F = \begin{bmatrix} \beta_{E0}(0)\,S_0 & \beta_{I0}(0)\,S_0 & \beta_{W0}(0)\,S_0 \\ 0 & 0 & 0 \\ 0 & 0 & 0 \\ 0 & 0 & 0 \end{bmatrix} \qquad V = \begin{bmatrix} u_1 & 0 & 0 \\ -\alpha(1-p) & u_2 & 0 \\ -\alpha p & -q & 0 \\ -\xi_1 & -\xi_2 & \sigma \end{bmatrix}$$

Here $u_1 = \alpha + \gamma_1 + \mu$ and $u_2 = q + \gamma_2 + \mu$. Then, R_0 of the given model will be the spectral radius of the next generation matrix FV^{-1} which is

$R_0 = \rho(FV^{-1}) = R_E + R_I + R_W$

Where

$R_E = \frac{\beta_E(0) S_0}{u_1} = 1.33$

$$R_I = \frac{\alpha\,(1-p)\,\beta_I\,(0)S_0}{u_1 u_2} = 0.15$$

$$R_W = \frac{\beta_W\,(0)S_0}{\sigma u1}\left(\xi_1 + \frac{\xi_2 \alpha\,(1-p)}{u2}\right) = 0.13$$

It estimates the disease risk during the second period (COVID-19 era). The first two terms, R_E and R_I represent the role of human-to-human transmission routes from non-clinical and clinical infectious populations respectively. The third term, R_W characterizes the impact of the environment on the human transmission pathway through sewage contamination. Thus, we proceed as follows:

$$R_0 = 1.33 + 0.15 + 0.13 = 1.61$$

The values indicate that exposure to asymptomatic infectious population makes the highest contribution, followed by the infected population, and then the environment makes the lowest contribution. All of these values combined make R_0 almost equal to unity, indicating the persistence of the disease. Although the environment was found to play the least role in virus transmission, the rates were close enough to the rates of infected to susceptible populations, indicating that with low vaccination coverage and poor WASH infrastructure, the wild poliovirus contaminated environment can impact disease propagation.

Another important measurement is the effective reproduction number (R_{eff} or R_t), which is the expected number of new infections caused by infectious individuals, to which some individuals in the target population may no longer be susceptible. It is important to reduce this number to below one to control the spread of infection. In our case, our whole population was not susceptible; therefore, we calculated the effective reproduction number for the second time period using the derived value of the basic reproduction number.

$$R_{eff} = R_0\left(\frac{S}{N}\right)$$

As a result, a value of 0.12 for the effective reproduction number was obtained, indicating the effectiveness of current intervention strategies in reducing the number of susceptible populations in the country. This is because the value of R_{eff} is directly proportional to the magnitude of susceptible individuals in a target population, and when the number of at-risk individuals is high, the value of R_{eff} is greater than 1. When the susceptible population is lower, the value of R_{eff} is closer to 0, and the disease is contained.

Using the estimated values of the parameters through the model calibration, predictions for the occurrence of future polio cases in Pakistan could be made in the near future. We simulated the developed model considering that the transmission rate no longer increases monotonically. Following the current vaccination scenario and assuming that vaccination rates can keep missing children at the current proportion of nearly 1% every year, the prediction of future transmission scenarios **Figure 5 and 6** indicated that the transmission will remain endemic and that the number of reported cases will be lower than that previous years. The graph depicts that the model has better predictive ability with the expected polio cases for the year 2023 to be five with the maintained vaccination rate. On the other hand, the vaccination rate dropped in 2023 and reported cases were almost six in the same year closer to the model predictions (Mbaeyi et al. 2023; GPEI 2024). However, the number of asymptomatic infections remains a problem, as the graph indicates a continuous rise in latent infections as the susceptible population accumulates over the years.

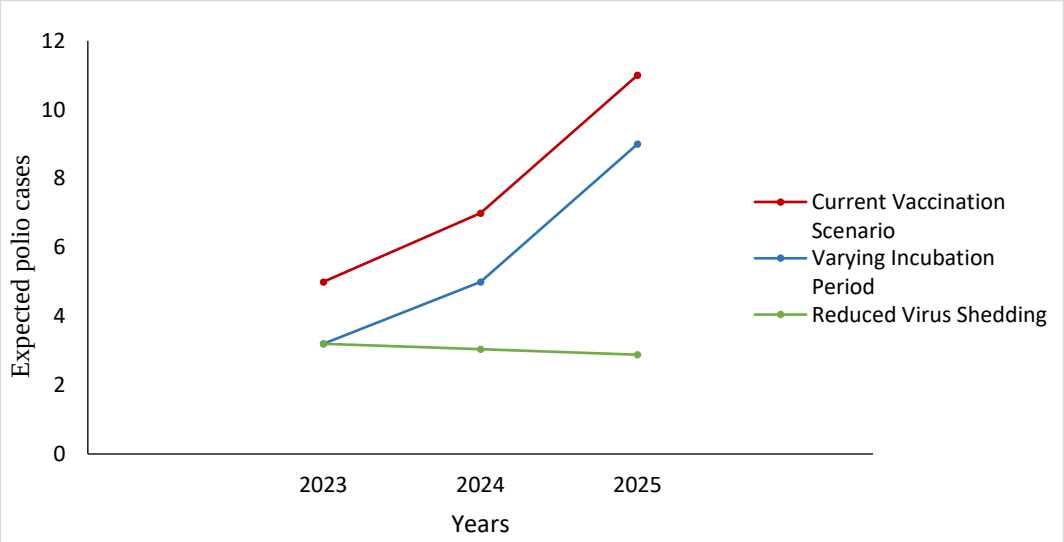

Figure 5. The expected number of polio cases from 2023-2025 with the ongoing immunization rates and when the incubation period reaches 21 days. The green line depicts the decreasing incidence rate with the reduction in the virus shedding rate of the asymptomatic population.

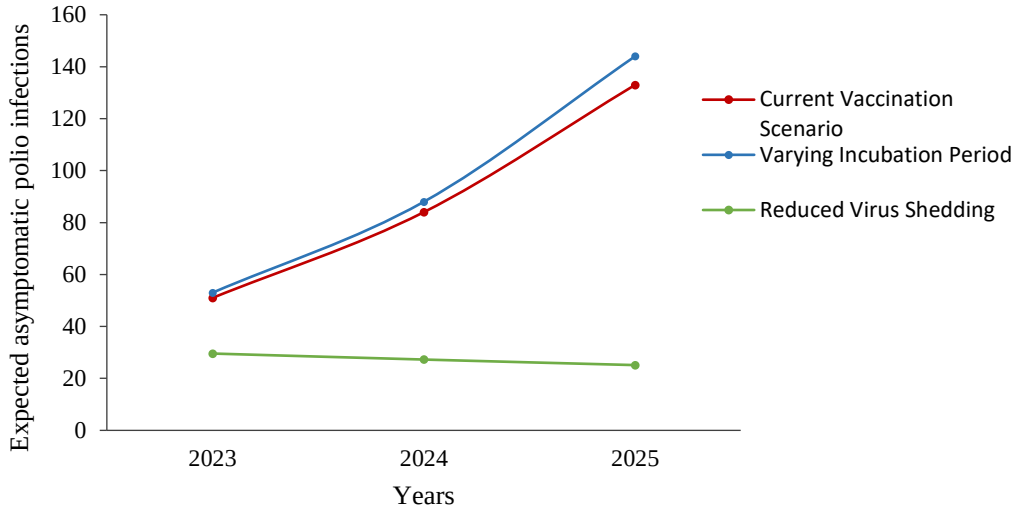

Figure 6. The expected asymptomatic polio infections from 2023-2025 with the ongoing immunization strategies and when the incubation period reaches 21 days. The green line depicts the reduction in asymptomatic infections with reduced virus shedding.

Simulations with varying parameters

The values of the model parameters can vary due to various factors, including environmental conditions, the evolution of population immunity, and changes in population movement patterns across the country. Here, the influence of the incubation period and virus shedding rate of the asymptomatic population was estimated based on the proportion of reported cases. **Figure 5** indicates that a higher incubation period leads to a lower number of reported cases. It has been observed that the poliovirus incubation period can range from 7-21 days or even up to 35 days. It also indicated that with an increase in the virus incubation period, the number of latent infections will increase as the virus takes longer to reach the symptomatic phase. Thus, there will be more asymptomatic individuals, posing a threat to the susceptible population. **Figure 6** presents the scenario when the poliovirus incubation period reached 21 days and the number of latent infections was higher. This increases the threat of silent transmission of poliovirus in the community, as sub-clinical infections are a major source of silent circulation of the virus. The graph depicts the failure of vaccination campaigns to achieve the target vaccination rates. The increase in virus incubation can be attributed to reduced or partial immunization. Incomplete vaccination due to various extrinsic and intrinsic factors leads to infections with longer incubation periods. This increase in the incubation period and asymptomatic infections, along with the resultant decrease in the number of reported cases, presented a scenario of silent circulation. This increases uncertainty in public health measures.

This is particularly important in the case of isolated under-vaccinated sub-populations which pose a threat to the entire community. This can also be detected through environmental surveillance. The presence of positive samples indicated silent transmission of poliovirus throughout the country. This situation suggests that more targeted intervention efforts are required to vaccinate under-vaccinated partitioned sub-populations.

Another scenario for reducing the virus shedding rate in asymptomatic individuals was tested by changing this parameter. A significant decline in the number of asymptomatic infections was observed. In addition, the curve for the proportion of the infected population flattens over time with the reduction of the virus shedding rate by the sub-clinical infectious population. The shedding rates for the exposed and reported infections were considered equal. **Figure 5** and **6** represent the expected reported cases and latent infections to occur in the next three years, respectively, when the virus shedding rates of the infected and exposed are equal. This indicates the importance of higher vaccination coverage and the need to consider population movement patterns in targeted immunization campaigns. This will also help reduce the number of positive environmental samples with WPV in the entire country. The graph suggests that with a reduction in the virus shedding rate of latent individuals, the number of reported cases of poliovirus will continue to decrease until consistent intervention strategies completely vanish the infected individuals from the community. This will ultimately help eradicate the virus from the country.

Discussion

In this study, an ordinary differential equation-based deterministic model was developed for poliovirus persistence in Pakistan. The model applies the concept of time-dependent transmission rates of polio infections. This assumption is usually considered for seasonal infections and takes into consideration the periodicity of the occurrence of a disease (Thompson et al. 2019). Moreover, the role of poliovirus-contaminated sewage water in the spread of infection was considered. In this model, both direct and indirect transmission routes, considering human-human and environment-human transmission, were incorporated. The period of 2017-2022 was considered for the numerical simulations and model validation. The considered time domain of 6 years was divided into two 3-year time periods: variable transmission rates that increase monotonically with time in Period 1, and variable transmission rates that are shaped by disease prevalence and human behavior in Period 2. The model was applied to the WPV1 case data from Pakistan. The results of the present data fitting approach

based on different transmission rates in different time periods show a better performance than that based on the standard approach of using uniform, constant transmission rates throughout the entire time domain.

Martinez-Bakker et al. (Martinez-Bakker et al. 2015) previously conducted an analysis on the ecology of polio epidemics in the mid-20th century. The findings revealed that prior to the introduction of vaccination, only approximately 6% of infections were officially reported. The primary cause of these epidemics was the rise in birth rates. The study ultimately concluded that for vaccination campaigns to be more effective, it is crucial to consider population demographics and the seasonality of infections. Conversely, our modelling results indicate that as we approach the era of polio eradication, population demographics play an increasingly significant role in the occurrence of polio infections in Pakistan. The authors acknowledge that subclinical infections are more prevalent today than in the pre-vaccine era, which aligns with our current findings. Our model simulations predicted that the virus will continue to transmit in the presence of immunocompromised children. Therefore, it is imperative to monitor the movement patterns of asymptomatic unvaccinated individuals capable of spreading infections throughout the country. The rates of pathogen transmission are determined by two critical factors: the frequency of contact between susceptible and infectious individuals and the duration of contact and immunity within the population (De Cao et al. 2014).

Molodecky et al. (Molodecky et al. 2017) performed spatiotemporal analysis of routine surveillance data for wild poliovirus in Pakistan. The findings indicate that movement patterns are not as influential in predicting future polio cases in the country as the virus is mostly restricted to certain areas. However, our results revealed that movement patterns are major contributors to the constant expansion of the virus in Pakistan and can contribute significantly to accurate predictions of future polio cases in the country. This is evident from the reduction in the number of cases during the COVID-19 lockdown, when movement was restricted and transmission was assumed to no longer increase monotonically.

Browne et al. (Browne et al. 2015) investigated the impact of routine and supplementary immunization activities, as well as seasonality and environmental transmission, on the effective reproduction number for poliomyelitis. The study concluded that migration rates can significantly affect the overall reproduction number and optimal vaccine strategies. This emphasizes the importance of synchronizing pulse (supplemental) vaccination strategies and suggests that supplementary immunization, considering complete indirect virus transmission

through the environment, would be most effective in reducing the reproduction number. Our simulation-based calculation of the effective reproduction number supports the effectiveness of national immunization strategies against poliovirus in Pakistan as it shows a decreasing trend in the incidence of new cases. Furthermore, our study considered both direct and indirect routes of virus transmission. The calculated effective reproduction number suggests that supplementary immunization campaigns, when combined with spatiotemporal analysis of routine surveillance data, will ultimately lead to eradication.

The proposed model can be further enhanced by incorporating spatial data on vaccination coverage and environmental surveillance results. This will enable the prediction of future polio infections and the allocation of timely resources across the country to stop the transmission of the virus. However, the study did not consider population demographics, such as movement patterns, age structure of the susceptible population (Mach et al. 2014), population density, and migration rates. Additionally, the modelling results suggest that identifying asymptomatic infected populations is crucial for effective eradication efforts. Therefore, the model can be modified to explicitly include the demographics of the entire vulnerable population in Pakistan. This indicates specific characteristics such as transmission rates, paralysis rates, incubation period, and time to recovery. The shedding rate of the virus in the target population may also be affected by the OPV vaccination status (Brouwer et al. 2022). Furthermore, the model application did not consider the evolution of wild poliovirus in Pakistan over time. Consequently, it may not accurately reflect the infection prevalence in the distant future, as disease features can vary significantly over time. By including such dynamics associated with persistent virus transmission in the country, the modelling results can be improved and intervention strategies can be optimized to achieve eradication.

Conclusion

The transmission of wild poliovirus type 1 is expected to remain low in Pakistan which is subject to high vaccination coverage. The time-dependent transmission rates assumption for poliovirus spread in the country has a better predictive ability than the constant transmission rate models. Our modelling framework can be further enhanced by incorporating spatial data on immunization and routine surveillance to predict future cases in Pakistan and allocate preemptive measures. Furthermore, the model concluded that indirect virus transmission through the fecal-oral route had the least impact on the disease prevalence in Pakistan. The findings of this predictive model are important for eliminating the spread of wild poliovirus

from the remaining endemic countries (Pakistan and Afghanistan) by enhancing the activity of the Global Polio Eradication Initiative.

Statements and Declaration

Compliance with Ethical Standards

The manuscript did not involve any human or animal participants therefore, it did not require approval from the ethical board.

Ethical Approval

The authors certify that they complied with the Principles of Ethical Publishing Rules.

Informed Consent

The data reported were derived from studies already published and quoted in the reference list. Those papers mentioned informed consent that, depending on the studies, was implied to participate in the study, verbal or written, or a combination of these variants during the follow-up.

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