Brief Original Article

A mathematical modeling approach to measure the probability of HIV-1 transmission for different high-risk groups of Pakistan

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Abstract
Introduction: Since 2010, the number of new HIV-1 cases has declined by 30% globally, however, in few countries, such as Pakistan, the cases have continued to increase, where the country witnessed a 57% increase in the number of new infections between 2010 and 2020. The HIV-1 epidemic in Pakistan is concentrated in certain high-risk groups, however, it is unknown which high-risk group has a higher likelihood of transmitting HIV-1 infections to vulnerable populations. This study aimed to apply mathematical probabilistic modeling to estimate the probability of HIV-1 transmission for different high-risk groups of Pakistan.
Methodology: MATLAB software was used to conduct probabilistic modeling (chance estimation) of HIV-1 transmission for different high-risk groups of Pakistan, and also draw a comparison between Pakistan and different high- and low- HIV-1 prevalence countries.
Results: Our results revealed that Pakistan overall had the lowest probability of HIV-1 transmission as compared to other countries included in this study; however, within Pakistan, certain high-risk groups such as people who inject drugs (PWID) and the region of Larkana exhibited a high probability of HIV-1 transmissions.
Conclusions: Our study suggests that the concentrated HIV-1 epidemic in Pakistan has a high likelihood of expansion from certain high-risk groups to other vulnerable populations. Further studies to understand the socio-epidemiological factors driving the expansion of the HIV-1 epidemic within the country will guide specific HIV-1 intervention strategies to control the spread of HIV-1 from high-risk to other vulnerable populations.

Introduction

Human Immunodeficiency Virus 1 (HIV-1) is a major public health challenge globally and is currently responsible for more than 37 million infections worldwide [1]. Sub-Saharan Africa has the highest burden of HIV-1, where the infection is predominantly transmitted through heterosexual contact [2]. In contrast, in Asia, Latin America, and the Caribbean, hetero- and homo-sexual contact and drug-use-related transmissions are the primary HIV-1 transmission modes [3]. Estimates from 2018 suggest the HIV-1 prevalence to be 54% in Eastern and Southern Africa, 16%, in Asia and the Pacific, and 13% in Western and Central Africa, where Eswatini, formerly known as Swaziland, has the highest prevalence in the world i.e. 27.3% [4].

Globally, the number of new HIV-1 infections has decreased significantly, owing to measures taken by different HIV/AIDS control programs, awareness campaigns, and the advent of antiretroviral therapy [4]. However, in countries such as Pakistan, the number of new HIV-1 cases has proportionally increased over the years, with a nearly 57% increase in the number of new infections between 2010 and 2020 [4].

In Pakistan, HIV-1 exists as a concentrated epidemic in several high-risk groups, such as men who have sex with men (MSMs) and the person who inject drugs (PWID) [1,5,6]. More recently, Pakistan has witnessed several HIV-1 outbreaks on an unprecedented scale. For example, in March 2019, HIV-1 was reported in a single town in Sargodha, Punjab, where HIV-1 prevalence increased from 1% to around 13% in 6 months. Preliminary reports suggested that most of the patients in this outbreak were treated by the same unlicensed medical practitioner who tested positive for HIV-1 [7]. Similarly, in April 2019, another HIV-1 outbreak was reported in the Larkana district of Sindh, where more than 700 children were tested

positive for HIV-1 [8]. In Pakistan, poor infection control practices, low health awareness knowledge, and low treatment coverage has contributed to the rapid expansion of the HIV-1 epidemic [7]. Additionally, isolated reports have documented bridging of the epidemic between high- and low-risk populations [9], however, it is not known which high-risk groups are responsible or have a greater chance of spreading HIV-1 in the country.

Mathematical probabilistic models have been frequently used to predict HIV/AIDS transmissions [10]. These models consider factors such as high-risk behaviors, the estimate of the HIV-1 prevalence, etc. to model the spread of HIV-1 infection and also predict future cases that may arise within a community or country [11]. A Tanzanian study, for example, developed and analyzed a nonlinear mathematical model to study the effect of screening and treatment on transmission of HIV/AIDS infection in a population [12]. Similarly, a 2013 study from Pakistan, used the Estimation and Projection Package (EPP) developed by UNAIDS to analyze past and future patterns of HIV-1 emergence among the high-risk populations [13].. Public health researchers can effectively apply and utilize mathematical probabilistic modeling to identify which high-risk groups have the greatest likelihood of transmitting HIV-1, and subsequently, use this information to devise effective interventional strategies that can slow down the spread of HIV-1.

In this study, probabilistic modeling was applied on available global and local (Pakistan) HIV-1 prevalence data to 1) estimate the probability of HIV-1 transmission in Pakistan and draw a comparison between Pakistan and different high- and low- HIV-1 prevalence countries, and 2) estimate which high-risk groups in Pakistan have the highest probability of transmitting HIV-1 infections. Such data is expected to be useful in devising specific HIV-1 intervention strategies to control the spread of HIV-1 from high-risk to other vulnerable populations.

Methodology

Prevalence data and assumptions

MATLAB software was used to calculate the probability (chance estimation) of HIV-1 transmission in Pakistan and different high HIV-1 prevalence (Eswatini, South Africa, and Namibia) and low HIV-1 prevalence (Italy and Sweden) countries. For the simulation, 10,000 trials were performed, where 'chance' of HIV-1 transmission in Eswatini, South Africa, Namibia, Italy, Sweden and Pakistan was assumed to be 0.272, 0.189, 0.138, 0.0030, 0.0020 and

0.0010, respectively, based on the reported prevalence of 27.20%, 18.90%, 13.80%, 0.30%, 0.20% and 0.10% [14,4]. Similarly, the probability of HIV-1 transmission (chance estimation) for different high-risk groups of Pakistan was performed assuming the 'chance' of HIV-1 transmission in people who inject drugs (PWID), Hijra sex workers (HSW), men who have sex with men (MSM) and Larkana (the epicenter of HIV-1 transmission in Pakistan) to be 0.394, 0.075, 0.11, and 0.27, respectively, based on the reported prevalence of 39.4, 7.5%, 11% and 27% [15-17]. For these simulations also, 10,000 trials were performed.

Assumptions for the probabilistic model

The model was run on three probabilistic assumptions:
- Each replication of the method comes about in one of two conceivable results: true or false.
- The likelihood of 'true' is the same for each replication.
- The replications are independent, meaning that a 'true' in one HIV-1-positive individual does not impact the likelihood of 'true' in another.

Probability P for n or more HIV-1 positive individuals is the outcome

Probabilistic model

$$P = 1 - \sum_{n=0}^{x} (mn) \, P^n (1-P)^{m-n}$$

Where "n", "m" and "P" are as follows:
"n" = number of HIV-1 positive individuals
"m" = the population or trials
"P" = the probability of n or more HIV-1-positive individuals

Results

For this study, mathematical probabilistic modeling was applied to calculate the probability of HIV-1 transmission in Pakistan and also draw a comparison between Pakistan and six high- and low- HIV-1 prevalence countries. The probability of HIV-1 transmission in Pakistan was found to be 0.417 (Figure 1A), which was the lowest as compared to other high- and low-HIV-1 prevalence countries. The highest probability of HIV-1 transmission was predicted for Eswatini (0.498), while the lowest probability was predicted for Sweden (0.44%).

In the next step, the probability of HIV-1 transmission for different high-risk groups of Pakistan was determined (Figure 1B). The results revealed the highest probability of HIV-1 transmission for Larkana

(probability = 1), followed by PWID (probability = 0.979). The probability of transmission was found to be lowest for MSM and HSW (probability = 0.49; Figure 1B).

Discussion

This study aimed to use probabilistic modeling to estimate the chances of HIV-1 transmission by different high-risk groups of Pakistan. Probabilistic modeling was conducted through MATLAB software and the projected HIV-1 transmission probabilities were compared with those reported for different high- and low-prevalence countries.

From the six selected countries, the highest probability of HIV-1 transmission (0.498) was estimated for Eswatini. This finding is in agreement with the true prevalence rates of HIV-1 in Eswatini, which is highest globally [18]. In Eswatini, the number of AIDS-related deaths has decreased by 35%, however, the country still struggles to control the rise in the number of new HIV-1 cases [4].

Figure 1. Binomial probability for HIV transmission.

The graph shows the probability of HIV transmission in **A)** selected countries with a high- and low- prevalence of HIV-1 as well as in Pakistan, and **B)** different high-risk groups of Pakistan. As indicated in the methods, for each simulation 10,000 trials were performed.
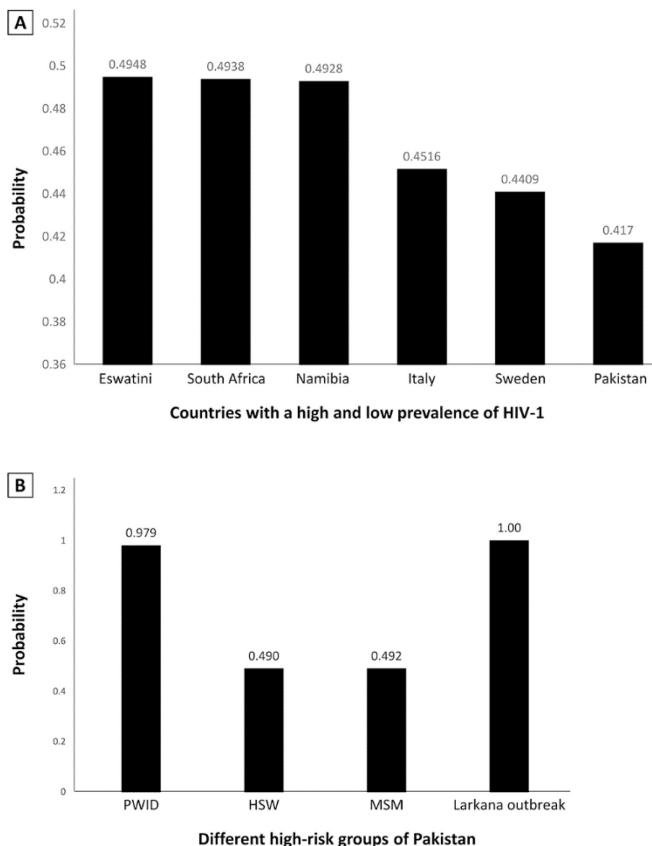
The transmission probability for Pakistan, based on population general population prevalence of HIV-1, was found to be the lowest (0.417) [4]. Pakistan is one of those countries, where general population prevalence is low (0.01%), however, HIV-1 exists as a concentrated epidemic in certain high-risk groups, such as PWID, MSM, and HSWs [15-17]. When chances of HIV-1 transmission were scaled according to the prevalence rates reported for several high-risk groups, the transmission probabilities increased to 1 (100%) for the region of Larkana and 0.97 (97.9%) for PWIDs. These findings are in agreement with the previously published reports that identify Pakistan among the four countries in Asia (other being Afghanistan, Bangladesh, Philippines) where the number of new HIV-1 infections has been increasing annually since 1990 [4,19]. Since 2010, there has been a 57% increase in the number of new HIV-1 infections [19]. One systemic review analyzing the HIV-1 epidemic in Pakistan reported very low prevalence rates of HIV-1 in the general population (0.04%), while the high prevalence of HIV-1 in certain high-risk groups, such as PWIDs (36.4%), HSWs (12%), and MSMs (17.5%) [20].

Despite the high prevalence of HIV-1 in these high-risk groups, the extent to which these high-risk groups are transmitting HIV-1 infection is not known [8]. Women in Pakistan are generally assumed to be at low risk for HIV-1 since they do not involve themselves in high-risk practices and do not exhibit promiscuous sexual behavior [21]. However, socially stigmatized MSMs tend to marry and hide their homosexuality from society, transmitting HIV-1 to their wives [21]. Similarly, children were no considered to be frequently affected by HIV-1 until the outbreak in Ratodero, Larkana in April 2019, where more than 700 children were diagnosed with HIV-1 within 3 months. Before March 2019, only 1423 children have registered with the National HIV/AIDS control program [8]. Our calculations suggest the likelihood of HIV-1 transmission for Larkana, an epicenter for HIV-1, to be 100%. This is in agreement with the published findings for the Larkana outbreak investigations, where the children reported in this single outbreak represented a 54% increase in the number of pediatric diagnoses over the past 13 years [8].

Conclusions

In summary, our study suggests that the concentrated HIV-1 epidemic in Pakistan has a high likelihood of expansion from certain high-risk groups to other vulnerable populations. The threat of HIV-1 epidemic expansion is real due to the low health

awareness, low treatment coverage, and poor infection control practices in Pakistan [8]. However, further studies to understand the socio-epidemiological factors driving the expansion of the HIV-1 epidemic within the country will guide specific HIV-1 intervention strategies to control the spread of HIV-1 from high-risk to other vulnerable populations.

Acknowledgements

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Conflict of interests: No conflict of interests is declared.