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ORIGINAL ARTICLE – OPEN ACCESS

Analysis of HIV Infection in Cyprus Using a Mathematical Model

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ABSTRACT

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Objective: The Mediterranean island of Cyprus has a high rate of human transit as a result of tourism, human trafficking, and migration, which could contribute to the rate of HIV infection. The island is divided into 2 states – the northern portion is mainly populated by Turkish-Cypriots, and the southern portion is populated by Greek-Cypriots. The aim of this study was to assess the dynamics of HIV infection in both segments of Cyprus using a mathematical model.

Materials and Methods: Data of HIV-positive individuals diagnosed during the period 1997–2018 in northern Cyprus were obtained from the Turkish Republic of Northern Cyprus Ministry of Health database, yielding a total of 129 cases, and data for the southern region, the Republic of Cyprus, were retrieved from a European Centre for Disease Prevention and Control (ECDC) 2013 report and ECDC/World Health Organization 2017 data. The total number of reported HIV infections was 1057. A mathematical model was used to evaluate the current and future HIV infection rate.

Results: Stability analysis of the equilibrium point – disease-free or endemic – was conducted using the Lyapunov function. The basic reproduction number, represented as R_0, is a measure of the potential for disease spread and serves as a threshold for stability. The R_0 value was 0.83 in northern Cyprus and 0.040 in southern Cyprus. An R_0 indicated a disease-free equilibrium.

Conclusion: The calculations suggest that there is no current HIV epidemic on either part of the island; however, the model predicted a significant increase in the near future.

Keywords: Analysis, HIV, Cyprus, epidemic, mathematical model

INTRODUCTION

HIV infection remains a major global public health issue, with an estimated 37.7 million people reported to be living with HIV, according to statistics from 2018. Globally, there were also approximately 770,000 HIV-related deaths in the same year. This implies that, despite the significant progress made in HIV treatment with the use of antiretroviral drugs and prevention strategies, HIV transmission persists worldwide. It has been estimated that 1.7 million people were newly infected with HIV in 2018. Furthermore, it has been estimated that only 79% of infected individuals know their HIV infection status; the remainder who are unaware may spread the infection. Key populations at increased risk of acquiring the HIV infection include intravenous drug users, prisoners, lesbians, gays, bisexuals, transgender individuals, and sex workers and their clients (1).

Cyprus is an island located at the approximate center of 3 continents, namely, Europe, Asia, and Africa. In part due to this geographical location, it attracts both legal and illegal migration. Illegal migration has grown in part due to the economic and political situation of neighboring countries. The highly indented coastline of Cyprus is a valuable characteristic for human trafficking. Cyprus is a destination country for men, women, and children who are trafficked for forced labor and sexual purposes (2, 3).

Cyprus is divided into 2 states. The Turkish Republic of Northern Cyprus (TRNC) is mainly populated by Turkish Cypriots, and the Republic of Cyprus (RoC) in the south is populated by Greek Cypriots (4). Reports indicate that the Greek Cypriot authorities meet the minimum standards of efforts to eliminate human trafficking, whereas the Turkish Cypriot authorities are deficient in this respect. Women subjected to sex trafficking in Cyprus were primarily from Eastern Europe, India, Vietnam, and sub-Saharan Africa, where HIV infection rates are high. Prostitution is illegal, and the Turkish Nightclubs and Similar Places of Entertainment Law of 2000 established a legal framework related to the problem of sex trafficking in the TRNC, however, enforcement is weak. This law provides that clubs may only provide entertainment such as dance performances, however, women hired to work as dancers, hostesses, or barmaids, etc., are often forced into sex work. In 2018, 351 women were reported to working with a permit for this type of work in the TRNC. The women were predominantly from Moldova, Morocco, and Ukraine, as well as Belarus, Russia, and other countries. The published figure does not include the number of unreported illegal employees. In addition, it has been reported that some entertainment establishment

owners hire female college students to avoid limits on the number of employees, taxes, and monitoring (2). Although sex work is also illegal in the RoC, there is a similar situation that many women working in entertainment establishments engage in selling sex (5).

In 2018, almost 4,000,000 tourists visited the RoC and 1,800,00 visited the TRNC. Tourists in the RoC were primarily from the United Kingdom, Russia, Israel, Germany, and Greece, where the HIV infection rate per 100,000 is 7.9, 18.2, 4.5, 4.2, and 5.7, respectively. However, for the TRNC, in addition to visitors from the United Kingdom, Germany, Russia, as observed in the RoC, there were also visitors from Turkey, France, and Ukraine, where there is an HIV infection rate of 3.1%, 7.8%, and 33.7%, respectively (6–8). Furthermore, almost 90,000 foreign students study at higher education institutions in the TRNC, and there are approximately 21,000 in the RoC. Students from developing countries or with a lower income can be more vulnerable to acquiring HIV as a result of selling sex to earn money or lack of knowledge of sexually transmitted diseases (9, 10). The population of the island, estimated to be 286,257 in the north and 854,800 in the south, is growing and there are many international visitors (8, 11). Thus, there has been concern about the risk of an HIV epidemic in Cyprus. This collaborative study of mathematicians, microbiologists, and infectious disease specialists used a mathematical model to analyze the level of HIV infection in Cyprus.

A mathematical model and epidemiological surveillance data of any infectious disease can be used to evaluate the epidemic character of the specified disease. A mathematical model can also provide a prediction of disease dynamics. This can be very useful to the appropriate authorities in efforts to develop policies to control and prevent the spread of disease.

The Susceptible-Infected-Removed (SIR) model, a standard mathematical model used in epidemiology, was used in this study. The aim of this study was to study the dynamics of current HIV infection in Cyprus and to offer predictions of the future rate of infection.

MATERIALS and METHODS

No ethics approval was required to conduct this study since it did not include any patient sample collection or clinical trial data. All of the data used are referenced and were obtained in a literature review.

This study was conducted in Nicosia, Cyprus. The parameters required for the mathematical model were obtained from the TRNC Ministry of Health and State Planning Organization (Table 1) and the RoC Demographic Report, European Centre for Disease Prevention and Control (ECDC), and World Health Organization (WHO) data (Table 2) (5, 6, 8, 11).

The SIR model was used to study the level of HIV infection in the northern and southern regions of Cyprus. The population (N *(t)*) was subdivided into 3 components: *S* (t), susceptible individuals; *I* (t), HIV-infected individuals; and R *(t)*, removed individuals. It was assumed that susceptible individuals were not yet infected with HIV, but were at risk of acquiring the infection at any time; entry into this category was via birth and exit was through infection with HIV or natural death (any death not related to HIV). If a susceptible individual became infected with HIV, they were moved to the infected category. The removed component consisted of individuals who had died naturally or as a result of HIV. The schematic representation of the mathematical model is represented in Figure 1.

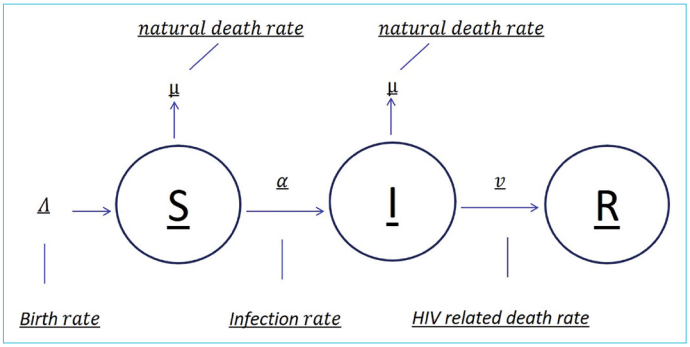

Figure 1. Schematic representation of the SIR mathematical model

The mathematical model used was adopted from a report presented by Saad et al. (12) and used a system of 3 nonlinear ordinary differential equations:

$$\frac{dS}{dt} = \Lambda - \frac{\alpha SH}{N} - \mu S$$

$$\frac{dH}{dt} = \frac{\alpha SH}{N} - (v + \mu)H$$

$$\frac{dR}{dt} = (v + \mu)H + \mu S,$$

$$S(t) > 0, \qquad H(t) \geq 0, \qquad and \quad R(t) \geq 0.$$

Equating the above equations to zero and solving simultaneously yielded 2 equilibrium points: Disease-free and endemic.

$$E_0 = \left(S_0 = \frac{\Lambda}{\mu}, H_0 = 0\right),$$

and

$$E_1 = \left(S_1 = \frac{v + \mu}{\alpha}, H_1 = \frac{\Lambda\alpha - \mu v - \mu^2}{\alpha(v + \mu)}\right).$$

The Lyapunov function was used to evaluate the following stability theorems. Proofs of the theorem are given in the work of Saad et al. (12).

Theorem 1. The disease-free equilibrium is stable when $R_0<1$.

Theorem 2. The endemic equilibrium E_1 is stable when $R_0\geq1$.

It is important to note that this is an existing model used to conduct a global stability analysis of HIV using the Lyapunov function (12). The next generation matrix method resulted in:

$$F = \begin{bmatrix} 0 \\ \alpha SH \end{bmatrix} \qquad V = \begin{bmatrix} \alpha SH + \mu S \\ (v + \mu)H \end{bmatrix}$$

$$f = \partial F(E_0) = \begin{bmatrix} 0 & 0 \\ \alpha S_0 & 0 \end{bmatrix} \qquad u = \partial V(E_0) = \begin{bmatrix} \mu & \alpha S_0 \\ 0 & v + \mu \end{bmatrix}$$

The basic reproduction number is the dominant eigenvalue of the fv^{-1}:

$$R_0 = \frac{\alpha\Lambda}{(v + \mu)\mu}$$

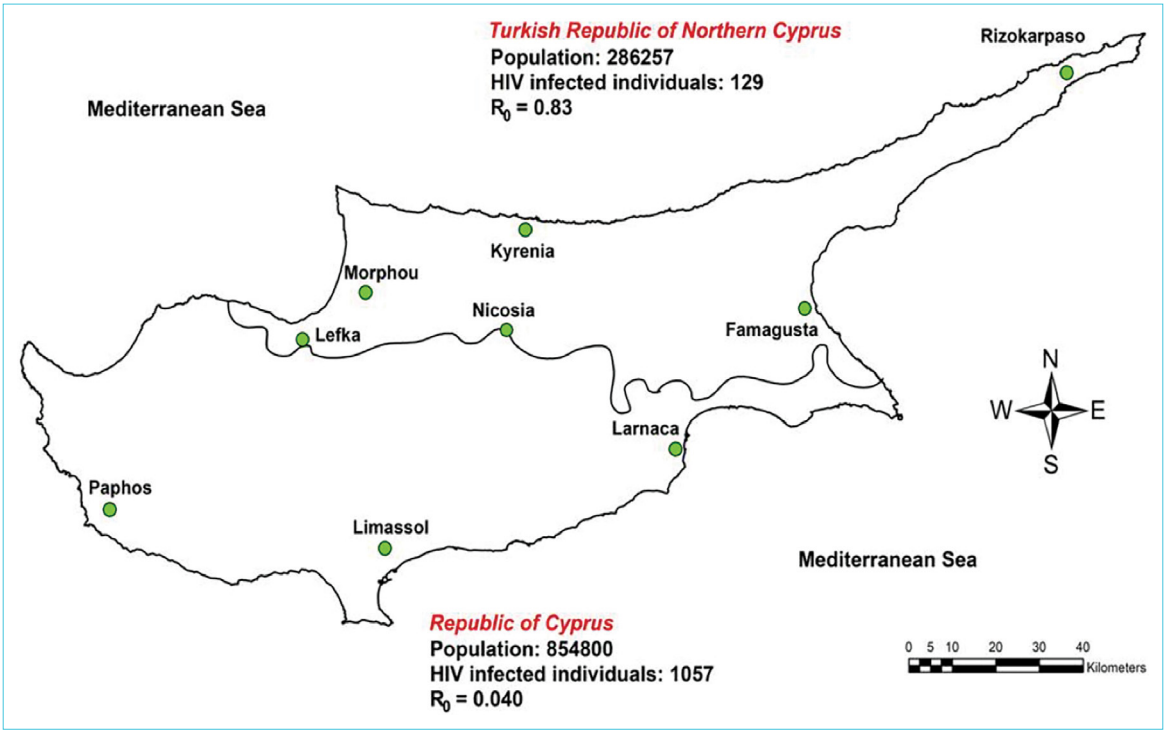

Figure 2. The mathematical calculations using official data indicated that there is currently no HIV epidemic in either part of the island

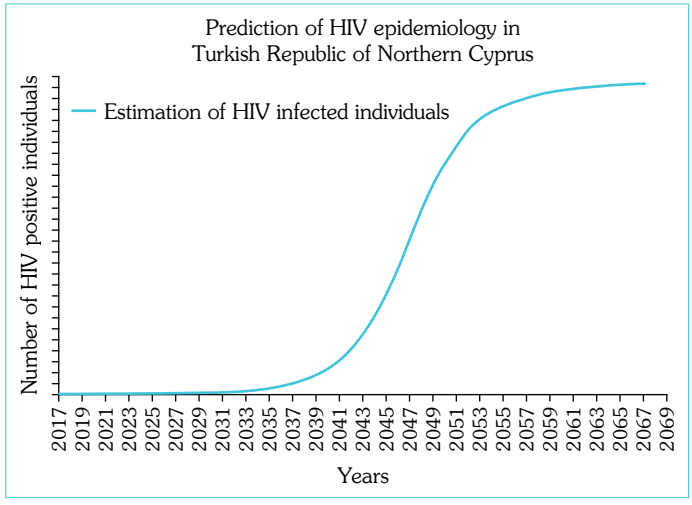

Figure 3. Prediction of HIV incidence in the Turkish Republic of Northern Cyprus for 50 years beginning in 2017. A dramatic rise in infection is expected in 2031 that will continue until 2055 before reaching a plateau

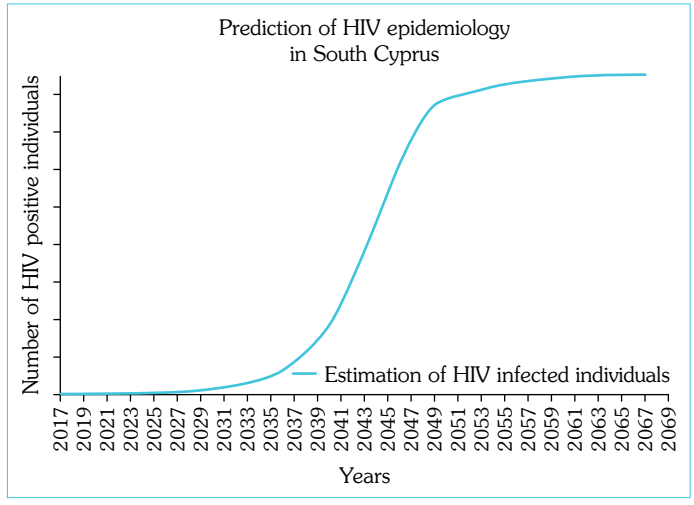

Figure 4. Prediction of HIV incidence in the Republic of Cyprus for 50 years beginning in 2017. A dramatic rise in infection is expected in 2028 that will continue until 2049 before reaching a plateau

The aim of this study was to utilize the model and basic reproduction number previously described (12) to study the dynamics of HIV infection in Cyprus (north and south).

The mathematical model used consisted of 2 equilibrium points: disease-free and endemic. R_0 reflects the number of individuals who could be infected with a particular disease by a single infectious person in a completely susceptible population, and therefore, the threshold. If the R_0 calculated using the mathematical model is equal to or greater than 1 ($R_0 \geq 1$), epidemic is expected to occur; however, if the R_0 is less than 1 ($R_0 < 1$), an epidemic is unlikely to occur.

Input variables and parameters used for the mathematical model were real data obtained from the respective government authorities as well as data published by the ECDC and the WHO (5, 6, 8, 11).

RESULTS

The basic reproduction number for calculated for the TRNC and the RoC was 0.83 and 0.040, respectively. This result indicates that there is no current HIV epidemic in either part of the island (Fig. 2). However, a simulation created using MATLAB software

Table 1. The variables and parameters of the Turkish Republic of Northern Cyprus (TRNC) used in the analysis

Variable/parameter	Description	Value
N	Total population	286.257
S	Number of susceptible individuals	129
I	Number of HIV-infected individuals	0.0013
Λ	Birth rate	0.004
μ	Natural death rate	0.0451
Λ	Infection rate	0.0451
V	Death rate due to infection	0.013699

Data sources: Hard copy 2018 report obtained from the TRNC Ministry of Health upon request and (11)

Table 2. The variables and parameters of the Republic of Cyprus (RoC) used in the analysis

Variable/parameter	Description	Value
N	Total population	854.800
S	Number of susceptible individuals	853.743
I	Number of HIV infected individuals	1057
Λ	Birth rate	0.00137
μ	Natural death rate	0.0026
Λ	Infection rate	0.1237
V	Death rate due to infection	0.013699

Data sources: (2, 6, 8)

(MathWorks, Portola Valley, CA, USA) to predict future dynamics of HIV infection in the area in the next 50 years revealed a dramatic rise in HIV infection in the north beginning in 2031 (Fig. 3). The results for the RoC were similar, with an increase in the number of individuals infected with HIV beginning in 2029 (Fig. 4).

DISCUSSION

Mathematical models have become a very important tool in the study of the epidemiological character of infectious disease. Researchers have used this technique to study *Escherichia coli*, hepatitis B, and influenza, among other diseases (13–15).

We used a mathematical model to analyze the dynamics of HIV in the TRNC and the RoC. According to our model, there is no current HIV epidemic on the island of Cyprus; however, a predictive simulation of the future dynamics of the next 50 years suggested that within approximately 10 years, a rise in the number HIV-positive individuals can be expected between 2031 and 2055 in the TRNC, following a slightly earlier growth period of 2029 to 2049 in the RoC.

CONCLUSION

The results suggest that there is no current HIV epidemic in either northern or southern Cyprus. However, the simulation performed using a mathematical model indicated a rise in the number HIV-positive individuals within the next 10 years. Thus, this suggests that the relevant authorities in Cyprus need to take more stringent measures to curtail the spread of HIV infection. The present study illustrates the importance of the study of infectious diseases using mathematical models to reveal the epidemic character of a disease and the value of this information to policy-makers in order to prevent the spread of disease.

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Informed Consent: This study did not include any patient sample collection or clinical trial. All the data used is referenced and obtained via literature review.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept – EH, TŞ, MS; Design – NS, BK, FS; Supervision – EH, TŞ, MS, KS; Resource – KS, EH, TŞ, MS; Materials – KS, EH, TŞ, MS; Data Collection and/or Processing – KS, EH, TŞ, MS; Analysis and/or Interpretation – NS, FS, BK; Literature Search – NS, FS, BK; Writing – NS, FS, BK; Critical Reviews – NS, FS, TŞ, EH, MS, BK, KS.

Conflict of Interest: The authors have no conflict of interest to declare.

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