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HIV Spread Mathematical Model for Simulation of UNAIDS Goal to End AIDS in Sudan

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Authors' contributions

This work was carried out in collaboration between all authors. Author IEK designed the study, performed the statistical analysis, wrote the protocol and wrote the first draft of the manuscript. Author MARENO managed the analyses of the study. Author CY managed the literature searches. All authors read and approved the final manuscript.

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ABSTRACT

The present study highlights, HIV spread mathematical model which backing up UNAIDS goal to end AIDS in Sudan. We report our investigation, in mathematical modelling perspective about HIV spread, and suggest some possible measures in order to control the epidemic. UNAIDS goal includes a 90-90-90 target, by 2020, [90% of all people living with HIV (PLHIV) know their status, 90% whose status are known are expected to be under ART, and 90% of PLHIV under ART have viral load suppressed.] Another goal extends the mission to year 2030 in which UNAID aim to end AIDS. According to UNAIDS, by 2030 UNAIDS want to minimize to at least 90% of both new HIV infections and AIDS-related deaths compared to year 2010. In this article, achievement of the goal is possible with appropriate control of the basic reproduction number (R_0). When $R_0 < 1$, rate of new HIV infections decreases toward stabilizing disease free equilibrium (DFE). In contrast, when $R_0 > 1$ the endemic equilibrium stabilizes. We took Sudan as an example in the simulation. According to the model, PLHIV records from 2012 to 2016 in Sudan estimated $R_0 = 1.5012$. HIV

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spread had been growing since 2012. Although all values of $R_0 < 1$ would lead to stabilize DFE, Although for achieving UNAIDS goal, any $R_0 \leq 0.0620$ after 2016 onward is a better estimate to meet UNAIDS goal to end AIDS by 2030 in Sudan.

Keywords: UNAID goal to End AIDS; 90-90-90 target; HIV in Sudan.

1. INTRODUCTION

Acquired Immune-Deficiency Syndrome (AIDS) has become a severe infectious disease in both the developed and developing nations in recent days, now being considered as a world pandemic [1]. HIV transmissions among individuals is mainly due to non-infected individual allowing blood contamination or unsafe sexual contacts with infected individuals [2]. AIDS results from infection with Human Immuno-deficiency Virus (HIV). Mother-to-child-transmission (MTCT) victimize many newborns especially in developing countries [3]. Worldwide, Africa is the worst hit continent by the pandemic and Sub-Saharan Africa remains most severely affected. In 2015, nearly 1 out of 25 adults (4.4%) were living with HIV in sub-Saharan Africa, accounting for ~70% of the PLHIV worldwide [4,5].

1.1 UNAIDS Achievements

Global plan to combat AIDS by UN which was co-chaired by UNAIDS and PEPFAR in 2011, since then there have been improved results in line with the plan [6]. In 2015, six priority countries (Botswana, Mozambique, Namibia, South Africa, Swaziland and Uganda) met the Global Plan target of reducing mother-to-child transmission by 90%. Outside of the priority countries, Cuba became the first country to eliminate the mother-to-child transmission of HIV in the world during mid-2015. In 2016, Belarus and Armenia achieved the same feat while Thailand became the first country in the Asia and Pacific region to eliminate MTCT. As PMTCT is not 100% effective, elimination of MTCT defined as a reduction of transmission to such low levels which no longer constitutes a public health problem [7].

1.1.1 UNAIDS Goal to End AIDS by 2030

In 2014, UNAIDS proposed a new mission aiming to end AIDS epidemic by 2030. There are two dependent objectives viz., (1) a 90-90-90 target, required by 2020, 90% of all HIV-infected people will know their HIV status (3), 90% of those diagnosed with HIV infection will receive sustained combination of antiretroviral therapy (ART), and 90% of all under ART will have viral load suppression [8,9]. In addition, the mission is to reduce both new HIV infections and AIDS-related deaths by 90% from 2010 to 2030 [10].

The Republic of Sudan is a country situated in the Northern Africa. Sudan's first case of HIV infection was reported in 1986, while in 2011 the total number of cases reported was 2218, this widespread of HIV is influenced by poverty and illiteracy, including HIV infected refugees from neighboring countries who flee to Sudan due to conflicts [11].

The mathematical models of population dynamics of infectious diseases are useful in making future projections to help the public health sector to plan optimally, a solution for the problem [12]. Several researches aimed to describe the epidemic evaluation in single countries or in single specific geographical regions, [12, 13, 14, 15]. In 2013, Mahfouz et al. [11], endorsed the factor associated with HIV/ADIS in Sudan to assess participant's knowledge regarding HIV/ADIS and identified the factors associated with HIV/ADIS. According to their results, a number of diversity risk factors were associated with HIV/AIDS. It is worthwhile to mention that a holistic approach could be immediately change sexual-risk-relating behaviour. Interventions including sustained educational programs, promotion of condom, and encouragement of voluntary testing and active involvement of the country's political and religious leaders to alleviate this problem.

Rao, et al. [14], developed ordinary differential equation model to describe the evolution of HIV epidemic in Italy for years 2003-2025. They considered a single population of susceptible, without distinction of high-risk groups against the general population, and no accounts for the presence of immigration and emigration. Modelling their effects on both the general demography and dynamics of the infected subpopulations. To present intra-host disease progression, the untreated, infected population distributed over four compartments in case cade according to the CD4+ counts. Benefits of this change in the incidence rate, the rate of new AIDS cases and the rate of the death from AIDS have been reported.

Table 1. Description of abbreviations

Abbreviations	Description
AIDS	Acquired Immune-Deficiency Syndrome
ART	Antiretroviral therapy (treatment)
$CD4^+$	Cluster of Differentiation
DFE	Disease Free Equilibrium
ED	Endemic Equilibrium
HIV	Human Immuno-deficiency Syndrome
MTCT	Mother-to-child-transmission
PLHIV	People Living with HIV
TB	Tuberculosis
UNAIDS	Joint United Nations Program on HIV/AIDS
WHO	World Health Organization

Nyabadza et al. [15], introduced a model with two stages of infections in South Africa. The results assumed that susceptible individuals have access to Pre-exposure Prophylaxis (PrEp), and thereby prevent themselves from HIV, especially exposed to HIV once they stop taking oral PrEp. They discussed and proved the global stability of disease-free equilibrium and endemic equilibria, according to their result using of PrEp potentially reduces the number of new HIV infections, and the sample simulation confirmed their analytical results. Oladotun et al. [17], represents a mathematical model with two control variables, where the uninfected $CD4^+$T cells follows the logistic growth function and the incidence term is saturated with free virions. They use the efficacy of drug therapies to block the infection of new cells and prevent the production of new free virions. The study exhibited the existence of an optimal control pair and use of Pontryagin's principle to characterize the optimal levels of the two controls. According to their analytical results, the effectiveness of the model in maximizing the concentration of uninfected CD 4^+ T cells, minimizing the concentrations of infected cells and free virions in the body with a minimum dose of combination of drug therapies in order the adverse impacts associated with excessive use of drug. In contrast, minimizing the cost of treatment of which the simulations confirmed the numerical results quite indirectly.

We have organized the rest of this paper as follows. In Section 2, we formulate the mathematical HIV/AIDS model, and stability analysis of the model in Section 3. In section 4, we perform the computational simulations and sensitivity analysis of R_0. The Discussion of the results were represented in Section 5. Finally, the Conclusion is given in Section 6.

2. MATHEMATICAL MODEL

We modelled the spread of HIV in the population into five classes: Susceptible (S), Adults not under ART (I), Children under ART (T_c), Adults under ART(T), and Removed (A) class. Among the five classes, only S is free from HIV infection. Both I and T are infectious except that T are adults under treatment on ART. T_c are children born infected, with an average proportion assumption that they do not participate in the spread of HIV. A has all individual with full brown AIDS, under ART and needs attention from others for caring. An individual in A is unable to spread HIV as they assumed not able to participate sexual interactions. Once an individual enters into a removed class, an average has left with a year to live. Table 2 describes the definition of the parameters involved to articulate the interaction between classes. Fig. 1 is a schematic diagram illustrating the interaction amongst the five HIV classes.

The interactions in Fig. 1 assumed to follow the system of differential equations below:

$$\begin{cases} \frac{dS}{dt} = \Lambda - \beta_1 c_1 S\frac{I}{N} - \beta_2 c_2 S\frac{T}{N} - \mu S \\ \frac{dI}{dt} = \beta_1 c_1 S\frac{I}{N} + \beta_2 c_2 S\frac{T}{N} - (\delta + \mu)I \\ \frac{dT_c}{dt} = \theta_1 I + \theta_2 T - (\gamma + \mu)T_c \\ \frac{dT}{dt} = \delta I - (\nu + \mu)T \\ \frac{dA}{dt} = \nu T + \gamma T_c - (\alpha + \mu)A \end{cases} \quad (2.1)$$

$S(0) = S_0, I(0) = I_0, T_c(0) = T_{c_0}$, T (0) = T_0 and $A(0) = A_0$

Table 2. Parameters description of model

Parameter	Description
Λ	Recruitment rate
β_1	Contact rate between I and S
β_2	Contact rate between T and S
c_1	Average number of partners per individual for I
c_2	Average number of partners per individual for T
μ	Natural mortality rate
δ	Rate of transfer from I to T
θ_1	Average rate of infected newborns from I
θ_2	Average rate of infected newborns from T
γ	Removal rate T_c to A
α	Induced death rate due to AIDS
ν	Removal rate T to A

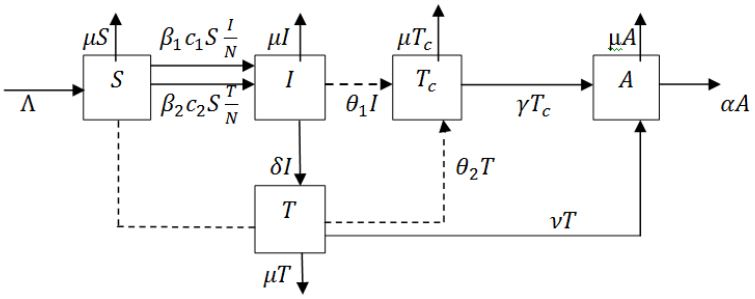

Fig. 1. Schematic diagram for HIV transmission

3. MODEL ANALYSIS

3.1 Feasibility of the Solution

The total population, $N(t) = S(t) + I(t) + T_C(t) + T(t) + A(t)$ suggested that

$$N'(t) = S'(t) + I'(t) + T_C'(t) + T'(t) + A'(t) = \Lambda - \mu N + (\theta_1 I + \theta_2 T) - \alpha A$$

$(\theta_1 I + \theta_2 T)$ is the total birth rate of HIV infected babies, αA is the total rate of death due to AIDS; If $(\theta_1 I + \theta_2 T) > \alpha A$, is total rate of newborn with HIV is greater than total death rate due to AIDS then $(\theta_1 I + \theta_2 T) - \alpha A > 0$ thus $N'(t) < \Lambda - \mu N$ so that $\lim_{t\to\infty} sup\, N(t) \leq \frac{\Lambda}{\mu}$ in this case the feasible region of the system (2.1) is positively invariant in Θ:

$$\Theta = \left\{(S, I, T_C, T, A): S + I + T_C + T + A = N \leq \tfrac{\Lambda}{\mu}, S > 0, I \geq 0, T_C \geq 0, T \geq 0, A \geq 0\right\} \quad (3.1)$$

Otherwise $(\theta_1 I + \theta_2 T) - \alpha A \leq 0$ so that $N'(t) \geq \Lambda - \mu N$. Solve the latter $N \geq \frac{\Lambda}{\mu}$.

3.2 Disease-free Equilibrium (DFE)

DFE of the system (2.1) is evaluated as $E_0\left(\frac{\Lambda}{\nu}, 0,0,0,0\right)$ and used to estimate the basic reproduction number (R_0) by next generation method.

$$R_0 = \frac{1}{2}\left[\frac{\beta_1 c_1}{(\delta+\mu)} + \sqrt{\left(\frac{\beta_1 c_1}{(\delta+\mu)}\right)^2 + \frac{4\delta\beta_2 c_2}{(\delta+\mu)(\nu+\mu)}}\right] \quad (3.2)$$

Theorem 1: DFE, $E_0\left(\frac{\Lambda}{\nu}, 0,0,0,0\right)$ of the system (2.1) is asymptotically stable if $R_0 < 1$.

Proof: Investigate the local geometrical properties of the DFE, $E_0 = (\frac{\Lambda}{\nu}, 0, 0, 0, 0)$ by considering the linearized system of ODE's (2.1). The Jacobian matrix evaluated at the DFE, ($J(E_0)$):

$$J(E_0) = \begin{bmatrix} -\mu & -\beta_1 c_1 & 0 & -\beta_2 c_2 & 0 \\ 0 & \beta_1 c_1 - (\delta + \mu) & 0 & \beta_2 c_2 & 0 \\ 0 & \theta_1 & -(\gamma + \mu) & \theta_2 & 0 \\ 0 & \delta & 0 & -(\nu + \mu) & 0 \\ 0 & 0 & \gamma & \nu & -(\alpha + \mu) \end{bmatrix} \tag{3.3}$$

The local stability of DFE may be determined from the Jacobian matrix (3.3), by evaluating its eigenvalues from the characteristic equation (3.3)

$$\begin{vmatrix} -\mu - \lambda & -\beta_1 c_1 & 0 & -\beta_2 c_2 & 0 \\ 0 & \beta_1 c_1 - (\delta + \mu) - \lambda & 0 & \beta_2 c_2 & 0 \\ 0 & \theta_1 & -(\gamma + \mu) - \lambda & \theta_2 & 0 \\ 0 & \delta & 0 & -(\nu + \mu) - \lambda & 0 \\ 0 & 0 & \gamma & \nu & -(\alpha + \mu) - \lambda \end{vmatrix} = 0 \tag{3.4}$$

Solve characteristic equation (3.4); eigenvalues are $\lambda_{1,2,3} = -\mu,\ -(\propto + \upsilon),\ -(\gamma + \upsilon)$ the rest $\lambda_{4,5}$ are from the quadratic equation:

$$\lambda^2 + \left[\nu + \mu - \left(\beta_1 c_1 - (\delta + \upsilon)\right)\right]\lambda - \left[\left(\beta_1 c_1 - (\delta + \upsilon)\right)(\nu + \mu) + \delta\beta_2 c_2\right] = 0 \tag{3.5}$$

By properties of quadratic equations (3.5)

$$\lambda_4 + \lambda_5 = -\left[\nu + \mu - \left(\beta_1 c_1 - (\delta + \upsilon)\right)\right] \text{ and } \lambda_4\lambda_5 = -\left[\left(\beta_1 c_1 - (\delta + \upsilon)\right)(\nu + \mu) + \delta\beta_2 c_2\right].$$

For stability of local DFE, requires that $\lambda_{1,2,3,4,5} < 0$. It is clear that $\lambda_{1,2,3} < 0,\ \lambda_{4,5} < 0$ also provided that $\lambda_4 + \lambda_5 < 0$ and $\lambda_4\lambda_5 > 0$. The latter is true in such condition that:

Choose $\frac{\beta_1 c_1}{\delta+\mu} < \min\{1 - \frac{\delta\beta_2 c_2}{(\delta+\mu)(\nu+\mu)}, 1 + \frac{(\nu+\mu)}{(\delta+\mu)}\}$, that means $\frac{\beta_1 c_1}{\delta+\mu} < 1$ and $\frac{\delta\beta_2 c_2}{(\delta+\mu)(\nu+\mu)} \ll 1$.

Note that: $\frac{\beta_2 c_2}{\delta+\mu} < \frac{\beta_1 c_1}{\delta+\mu} < 1$ and $\frac{\delta}{(\delta+\mu)} < 1$ so that $\frac{\delta\beta_2 c_2}{(\delta+\mu)(\nu+\mu)} \ll 1$.

The latter concludes that $R_0 = \frac{1}{2}[\frac{\beta_1 c_1}{(\delta+\mu)} + \sqrt{\left(\frac{\beta_1 c_1}{(\delta+\mu)}\right)^2 + \frac{4\delta\beta_2 c_2}{(\delta+\mu)(\nu+\mu)}}] < 1$.

3.3 Endemic Equilibrium Point of the Model

The model (2.1) has the endemic equilibrium

$$E_*(S^* = \frac{\Lambda}{\mu} - \frac{\delta+\mu}{\mu}I^*,\ I^*,\ T_c{}^* = \frac{\theta_1(\nu+\mu)+\theta_2\delta}{(\gamma+\mu)(\nu+\mu)}I^*,\ T^* = \frac{\delta}{\nu+\mu}I^*,\ A^* = \frac{\gamma[\theta_1(\nu+\mu)+\theta_2\delta]}{(\gamma+\mu)(\nu+\mu)} + \frac{\nu\delta}{(\nu+\mu)(\alpha+\mu)})$$

$$I^* = \frac{\Lambda(\alpha+\mu)(\gamma+\mu)[\mu\beta_1 c_1(\nu+\mu)+\delta\beta_2 c_2\mu-(\delta+\mu)(\nu+\mu)\mu]}{\beta_1 c_1 k_1 k_2 k_3 k_4 + \delta\beta_2 c_2 k_1 k_2 k_3 - [(\mu+{k_1}^2)k_2 k_3 k_4 + \delta\mu k_2 k_3 + (\theta_1 k_4 + \theta_2\delta)(k_2+\gamma)\mu + \nu\delta\mu k_3]} \tag{3.6}$$

Where: $k_1 = \delta + \mu,\ k_2 = \alpha + \mu,\ k_3 = \gamma + \mu,\ k_4 = \nu + \mu.$

3.4 Existence of Endemic Equilibrium

The fact that $I^* > 0$ justifies of the existence of the endemic equilibrium point, then from (3.6),

$$\mu\beta_1 c_1(\nu+\mu)+\delta\beta_2 c_2\mu-(\delta+\mu)(\nu+\mu)\mu>0 \iff 1<\frac{\beta_1 c_1}{\delta+\mu}+\frac{\delta\beta_2 c_2}{(\delta+\mu)(\nu+\mu)}.$$

It follows that $2<\frac{\beta_1 c_1}{\delta+\mu}+\frac{\beta_1 c_1}{\delta+\mu}+\frac{2\delta\beta_2 c_2}{(\delta+\mu)(\nu+\mu)}<\frac{\beta_1 c_1}{\delta+\mu}+\frac{\beta_1 c_1}{\delta+\mu}+\frac{4\delta\beta_2 c_2}{(\delta+\mu)(\nu+\mu)}$,

Assuming that PLHIV under ART have viral road suppressed and therefore far better resistant to the HIV transmission than PLHIV not under ART, then $\beta_1 c_1 \gg \beta_2 c_2$, so that $\frac{\beta_1 c_1}{\delta+\mu}>1$.

That is $2<\frac{\beta_1 c_1}{\delta+\mu}+\sqrt{(\frac{\beta_1 c_1}{\delta+\mu})^2+\frac{4\delta\beta_2 c_2}{(\delta+\mu)(\nu+\mu)}} \Leftrightarrow 1<\frac{1}{2}\left(\frac{\beta_1 c_1}{\delta+\mu}+\sqrt{\left(\frac{\beta_1 c_1}{\delta+\mu}\right)^2+\frac{4\delta\beta_2 c_2}{(\delta+\mu)(\nu+\mu)}}\right)=R_0$

4. NUMERICAL SIMULATIONS

Based on the data collected for PLHIV in Sudan, no information was reported regarding children who were born living with HIV. Therefore, the parameters for HIV infected newborn in this case are subjected to assumptions. Table 3 from unaids.org/en/regionscontries/countries/Sudan for estimating the parameters for the model.

4.1 Estimation of Parameters

We also estimated the model parameters using the least square methods by the aid of Mat-Lab. Table 4 represent the estimated parameters in plot the data in Table 3.

Information from Table 1 are plotted by the model using estimated parameters as depicted in Fig. 2(a), and 2(b).

Table 3. Records of HIV infections between 2012 to 2016 in Sudan

Category	Year				
	2012	**2013**	**2014**	**2015**	**2016**
PLHIV not under ART	43,300	44,300	45,140	46,780	47,400
PLHIV under ART (T)	2400 (5%PLHIV)	3500 (7%PLHIV)	4160 (8%PLHIV)	4320 (8%PLHV)	5600 (10%PLHIV)
Deaths due to AIDS (A)	2300	2500	2700	2900	3000
New HIV infections	5100	5100	5000	5000	5000
Total PLHIV	48,000	50,000	52,000	54,000	56,000
Susceptible (S)	37.652mil	38.45mil	39.348mil	40.176mil	41.124mil
Total Pop. (N)	37.7mil	38.5mil	39.4mil	40.23mil	41.18mil

Table 4. Parameters description of model

Parameter	Description
Λ	1500000
$\beta_1 c_1$	0.0650
$\beta_2 c_2$	0.0033
μ	0.0156
δ	0.0284
θ_1	0.0000
θ_2	0.0030
γ	0.0001
α	0.0001
ν	0.0800

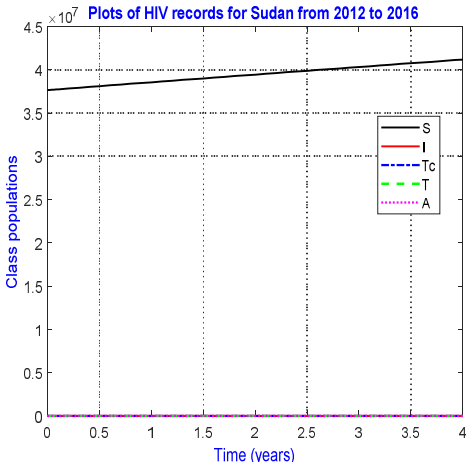

Fig. 2(a)

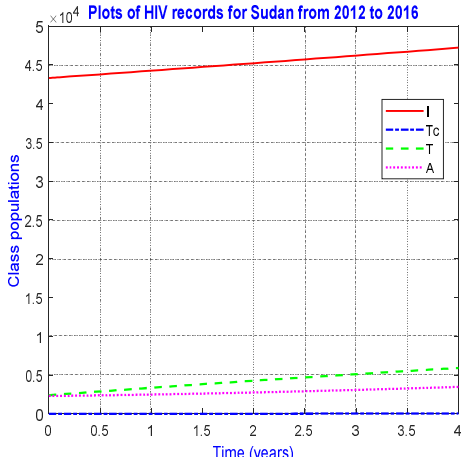

Fig. 2(b)

Whenever any Sudanese women are pregnant, knowing her HIV status is necessary. In addition, if infected, she is then obliged to start ART program. Based on this fact it is assumed that all PLHIV without considering ART are not bearing HIV infected newborns, therefore, the rate is estimated to become zero. The value of R_0 has been estimated as 1.5012 rendering to the growth of HIV spread.

4.2 Simulation of $\mathrm{SIT_CTR}$ Model

4.2.1 Expected HIV spread status 2016-2020

Based on the historical records as depicted in Fig. 2(a) and 2(b), the situation is extrapolated for the next four years from 2016 to 2020 (ref to Fig. 3(a) and 3(b)) to predict the HIV spread status in Sudan. This simulation will enhances our understanding whether the UNAIDS 90-90-90 target can be realized.

It is revealed that the number of PLHIV under ART are increasing every year, however this rate is not enough to suppress the rate of new HIV infections. Basing on the fact that $R_0 = 1.5012$ the number of PLHIV who are not under ART (I) are increasing every year, reflecting non-decreasing HIV infections rate, Fig. 3(a). Total PLHIV in 2016 was 56,000; this number is may increase by 2020 to about 60,000. Out of total PLHIV in 2020 on about 14% (8500) shall be under ART. This is a 4% increase compared to the PLHIV under ART in 2016, which was 10% (5600) of PLHIV.

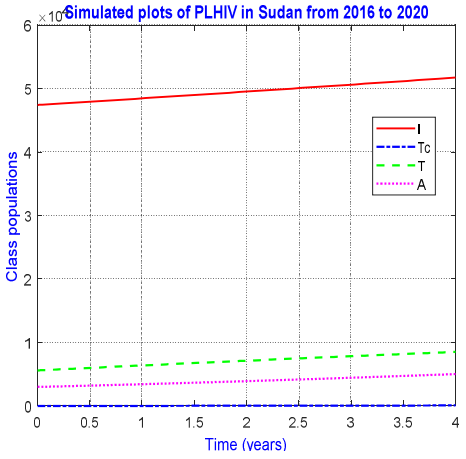

Fig. 3(a).

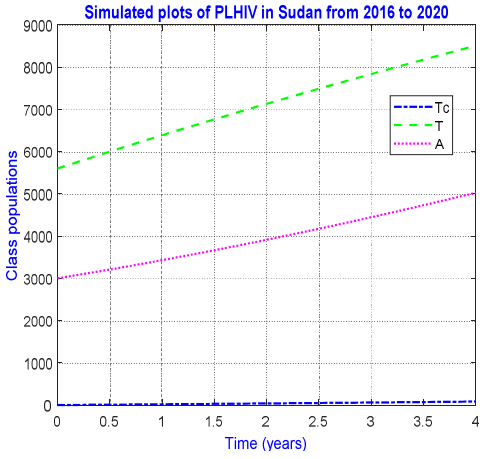

Fig. 3(b).

4.2.2 Expected HIV spread status 2016-2030

Failure to achieve the 90-90-90 target as depicted in Fig. 3 has a negative influence to anchor achievement of the goal to end AIDS by 2030 in Sudan. The simulation of HIV spread statuses from 2016 to 2030 in Sudan have been depicted in Fig. 3(a) and 3(b). Fig. 4(a) has a larger scale to ensure observation of classes including R classes. One of the expected outcome that amounts to success of UNAIDS goal to end AIDS by 2030 is that number of deaths due to AIDS that decrease to at least 90% during 2010-2030. However, deaths due to AIDS in 2010 and 2016 were estimated around 1700 and 3000 respectively, this number is expected to rise by 2030 to at least 13000 deaths. The number of deaths due to AIDS is increasing gradually and there is no room for decreasing percentage deaths due to AIDS. Consequently, the situation, feasibility to achieve the UNAIDS goal to end AIDS is jeopardized.

4.2.3 UNAIDS goal and future of AIDS spread in Sudan

The fact is that if the UNAIDS goal to end AIDS by 2030 is not appropriately addressed, for instance if it remains in the current HIV spread status then number of deaths due to AIDS is expected to increase every year. Among the four classes of PLHIV, number of people in R is the lowest. However, the simulation suggests that this is expected to escalate, and in 20 years from 2016 may grow larger than T class, ref. Fig. 5(a). If the situation is left unattended then as a natural tendency, it is expected that the R class's prevalence may grow larger than all classes in PLHIV as referred in Fig. 5(b).

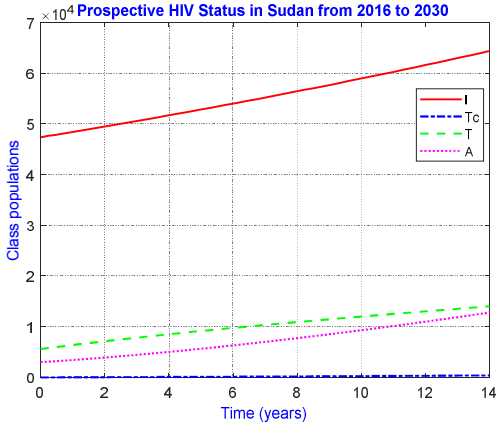

Fig. 4(a).

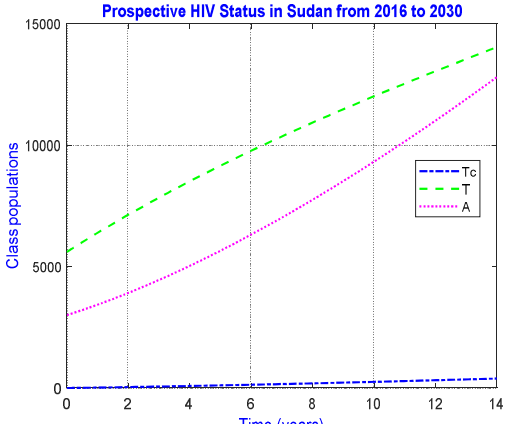

Fig. 4(b).

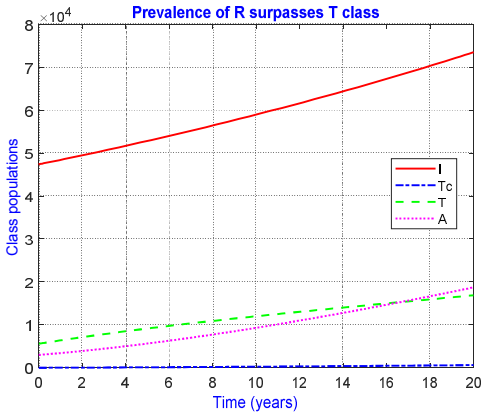

Fig. 5(a).

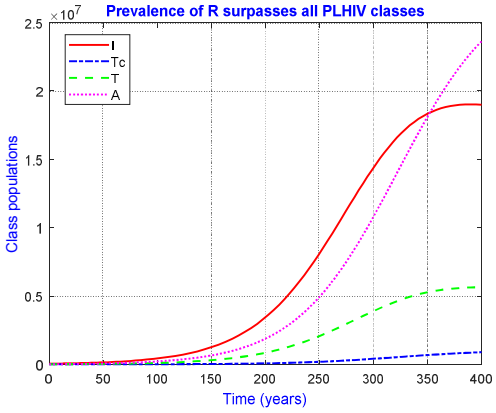

Fig. 5(b).

4.2.4 Equilibrium of the model

Equilibrium comes in as a response for the situation to restrain itself against further spread of the epidemic. The number of PLHIV is maintained to a constant number in some future. At this point, the model has an endemic equilibrium. All populations are constant in size including the susceptible class, as referred in Fig. 5.

4.3 Reverting HIV Spread Situation in Sudan

Any $R_0 < 1$ may revert the growing of HIV spread in Sudan to diminishing kind of infections. For instance, $R_0 = 0.7240$ reverts HIV infections as shown in Fig. 7; however, this may not lead to achieving the 90-90-90 target.

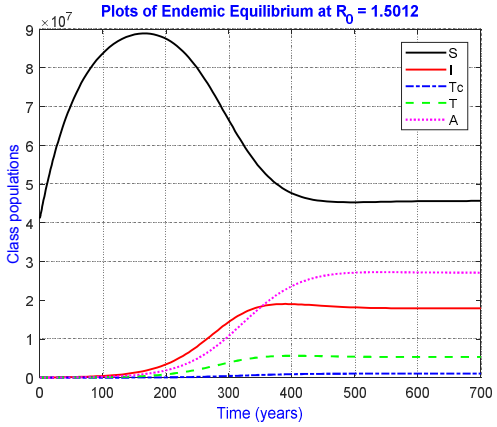

Fig. 6(a).

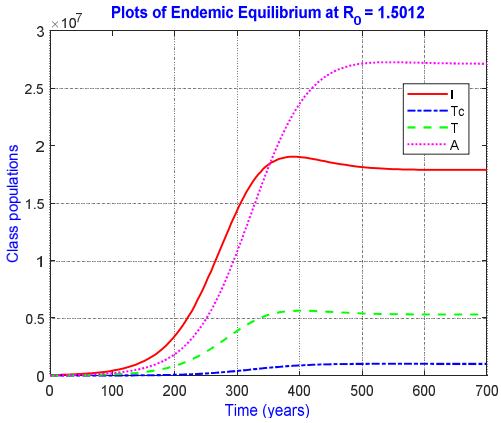

Fig. 6(b).

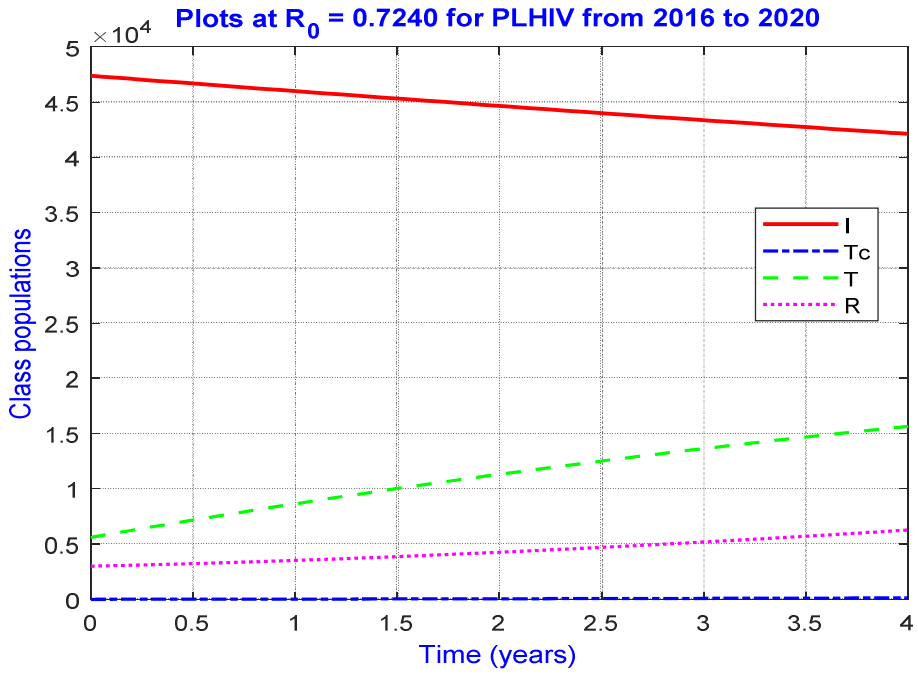

Fig. 7.

4.3.1 Value of R_0 in order to achieve the 90-90-90 Target in Sudan

Based on the situation prevailing in Sudan, it is estimated that a value of $R_0 \leq 0.0620$ would lead to achieved a 90-90-90 target, as depicted in Fig. 7(a). It is predicted that if the latter is maintained through 2020 to 2030, UNAIDS goal to end AIDS in Sudan is possible, as shown in Fig. 8(b).

Thus, based on the simulation; we estimated that 90% of PLHIV should be under ART by 2020 Fig. 8(a). The value $R_0 = 1.502$ from 2012 to 2016 suggested that by average 100 PLHIV were infected 150 individuals in their infectious period. With $R_0 = 0.0620$, 100 PLHIV by average infect six individuals in their life span as infectious. It is revealed that 96% of all PLHIV have been infected by HIV infection. Therefore, it is clear that at least 90% of PLHIV under ART will have their viral load suppressed by 2020.

In 14 years from 2016 (Fig 7b), provided that $R_0 = 0.0620$ is steadily controlled to 2030 the number of deaths due to AIDS will be reduced to about 2500 per year in compared to 3000 deaths per year in 2016, which is the highest since 2010 (in 2010 there were about 1700 deaths due to AIDS). In this study, we strongly recommend that; for Sudan to achieve UNAIDS goal, all PLHIV should start ART program, if possible free of charge to the victims like what the Botswana Government started in 2000s. Study also demonstrated that, Botswana is viable to achieve UNAIDS goal by 2030 provided to the prevailing of controlling HIV since 2016 (quote).

4.4 Sensitivity Analysis of the Basic Reproduction Number $(\mathbf{R_0})$

Sensitivity indices allowed us to estimate the relative change in a state variable when a parameter changes. In our simulation, we considered that a change of the state variable parallels with a change in the value of R_0. Since R_0 is a function of the parameters, then we can evaluate the relative sensitivity of R_0 for every parameter that R_0 depends on.

Definition: The normalized forward sensitivity of index for a variable, x which depends on a parameter, p denotes it as (γ_p^x) then defined

$$\gamma_p^x = \frac{\partial x}{\partial p} \cdot \frac{p}{x} .$$

So for $R_0(p) = \frac{1}{2}[\frac{\beta_1 c_1}{\delta+\mu} + \sqrt{(\frac{\beta_1 c_1}{\delta+\mu})^2 + \frac{4\delta\beta_2 c_2}{(\delta+\mu)(\nu+\mu)}}]$, the sensitivity index of R_0 , $\gamma_p^{R_o} = \frac{\partial R_o}{\partial p} \cdot \frac{p}{R_o}$; the parameter, p may replace by: $\beta_1 c_1$, $\beta_2 c_2$, δ or ν at a time.

Sensitivity indices of R_0: Table 5 is a list of sensitivity indices of $R_0(p)$ for the four parameters $\beta_1 c_1$, $\beta_2 c_2$, δ and ν. The parameter μ simply not considered as it is a natural death rate and therefore assumed to be constant. Evaluation of the sensitivity indices based on the parameters estimated in Table 4 for the data recorded in Sudan from year 2012 to 2016.

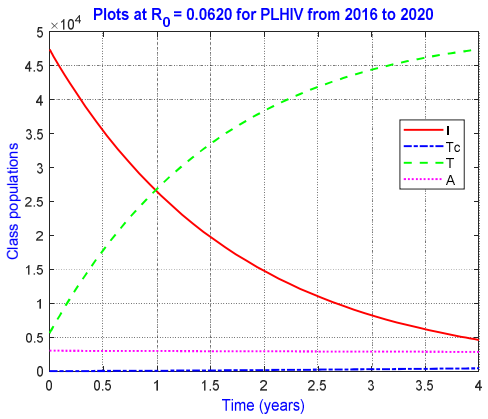

Fig. 8(a).

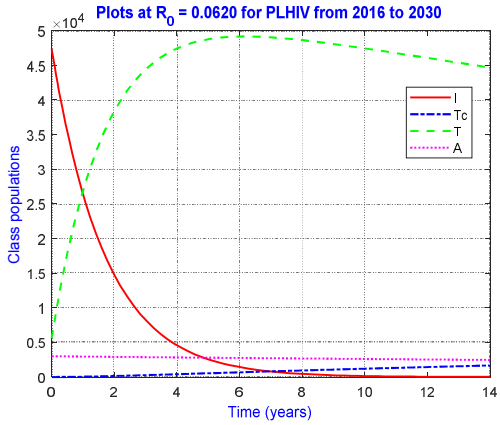

Fig. 8(b).

Table 5. Sensitivity indices of R_0

Highest sensitive first	Parameter	Sensitivity index
1	δ	-0.6293
2	$\beta_1 c_1$	+0.5164
3	$\beta_2 c_2$	+0.0098
4	ν	-0.0082

Like the ranking in Table 5, R_0 is relatively most sensitive to changes in the parameter δ and least sensitive for the parameter ν. The signs on the sensitivity indices indicate the directions of change. For example, R_0 increases with increase in $\beta_1 c_1$ and decreases with increase in δ and so on.

Fig. 9 is a graphical illustration of the sensitivity of R_0 for some selected interval of the parameters. Any increase in $\beta_1 c_1$ or $\beta_2 c_2$ leads to an increase in R_0, however, $\beta_1 c_1$ has a greater positive influence on R_0 in compared to $\beta_2 c_2$. For values of $\beta_1 c_1$ below a unit, there is approximately a linear relationship between R_0 and $\beta_1 c_1$, as shown in Fig. 9(a). In this particular, a unit change in $\beta_1 c_1$ leads to more than 20 units change in R_0. In contrast, R_0 is less sensitive to the variation in $\beta_2 c_2$. A unit change in $\beta_2 c_2$ has R_0 ranging in an interval below 3.5, as shown in Fig. 9(c).

In contrary to $\beta_1 c_1$ or $\beta_2 c_2$, an increase in δ or ν leads to a decrease in R_0. δ has a greater negative influence on R_0 than ν, [Fig 9(b)- 8(d)]. Increasing δ *or* ν from 0 to 1, decreases values of R_0 from 4.25 to about 0.25 for δ, Fig. 9(b) and decreases from 1.575 to about 1.49 for ν, [Fig. 9(d)]. This evidently suggests that increasing δ may better to control R_0 than increasing ν.

It should be noted that the sensitivity of R_0 is highest from δ when $R_0 > 1$. However, is most sensitive to $\beta_1 c_1$when $R_0 < 1$, Fig. 9(a) (c).

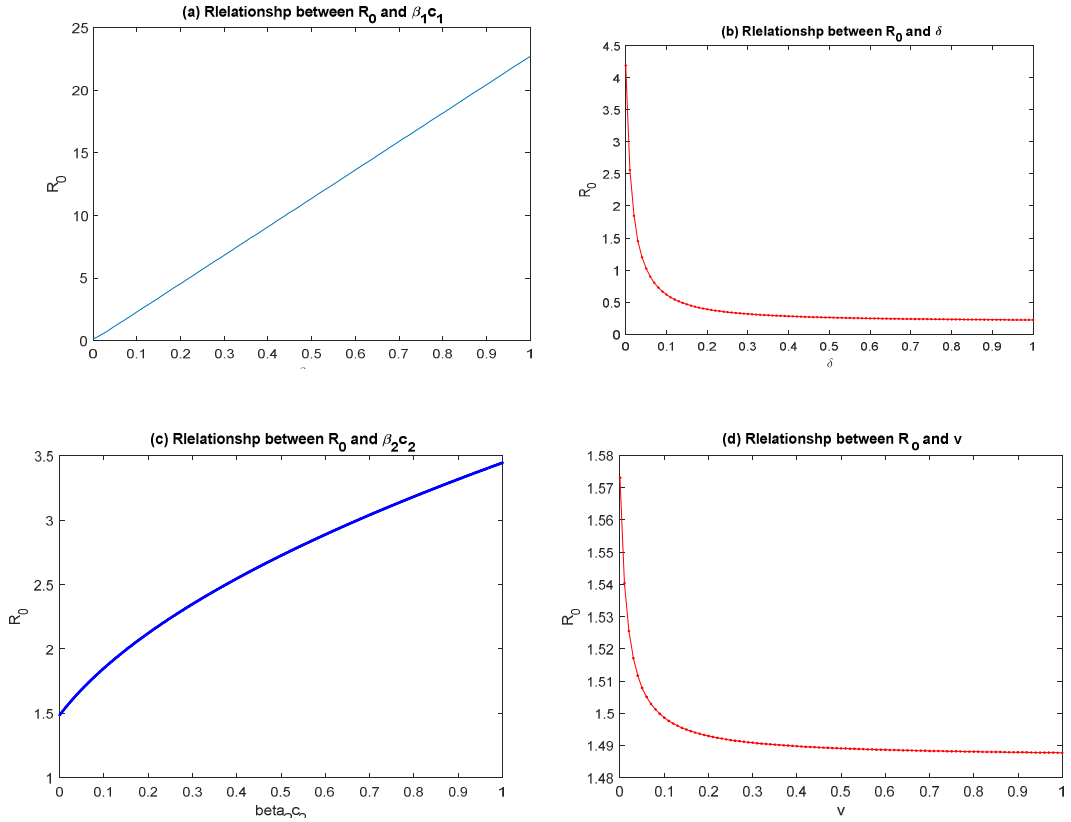

Fig. 9.

5. DISCUSSION OF THE RESULTS

Based on the simulation along with the sensitivity analysis of the basic reproduction number, we have reported that PLHIV without considering ART are primarily responsible for new HIV infections. In addition, if PLHIV under ART can follow the requirements during treatment; they are more resistant for HIV transmission and may suppressed viral load activity. This research resolves the following as recommendation to the Republic of Sudan. To prevent the increase in prevalence of HIV/AIDS, the government should be able to:

1) Provide guidelines for healthcare (HIV test, Medical care) with lower fees or free of cost, in line with supporting the Federal Ministry of Health as well as the State Ministry for every state of the country.
2) Schools, Universities, should educate all the students to understand how HIV/AIDS is spread and how they can protect against its infections; for instance, introducing some courses regarding HIV/AIDS be ministered by the Ministry of Education.
3) Providing some healthy programs to educate the women and society.
4) Educating the people in border and conflict areas.
5) Examine incoming and visitors from most affected countries, to be sure they are free of HIV/ADIS.

6. CONCLUSION

In this study, our main concern is to construct a model for HIV spread would help to understand control the epidemic. This is a dynamical system model, in this context named SIT_CTA. Basic reproduction number (R_0) guides the whole analysis of the model. Accordingly, there is a unique disease equilibrium for both DFE and EE. None of the backward bifurcation was existed and therefore the disease is controllable whenever $R_0 < 1$. $R_0 < 1$ leads to the extinction of the disease, thus stabilizing the DFE. In contrast, EE is stable when $R_0 > 1$. Sensitivity analysis of R_0 as a function of parameters suggested that when $R_0 > 1$ which is most sensitive to removal rate of PLHIV in a PLHIV under ART. In contrast, if $R_0 < 1$, then it is most sensitive to $\beta_1 c_1$. Based on these results the foremost step to revert an escalating HIV spread in Sudan of which $R_0 = 1.5015 > 1$ is to ensure that all PLHIV should immediately start ART so as stop or reduce HIV spread most effectively.

Moreover, we have investigated the applicability of the model by simulating HIV situation in Sudan following UNAIDS goal to end AIDS by 2030. The records since 2012 to 2016 for Sudan have $R_0 > 1$ as an estimation from the model. This reflects the fact that in Sudan, the spread of HIV by then had been increasing gradually. We did some simulations to predict the status of HIV spread associated with this R_0, it is evident that UNAIDS goal cannot be achieved, but values of $R_0 < 1$ have demonstrated reversing the spread towards extinction of the epidemic. For example, $R_0 = 0.7240$ decreases the rate of infections. However, for the sake of UNAIDS goal standards Sudan badly need $R_0 \leq 0.0620$. Challenges in Sudan includes the fact that majority of PLHIV are not under ART. Sensitivity analysis suggested that in compared to PLHIV not under ART, PLHIV under ART are relatively not responsible for the new HIV infections, Table 5. Accordingly, in order to achieve the UNAIDS goal against AIDS all PLHIV in Sudan should start ART. This demands both educating and cancelling institution to educate all people to know their status and start ART program appropriately. PLHIV under ART have to observe the rules associated with the program.

Nonetheless, this model does not address all features of the phenomenon in Sudan due to some limitations, the fact, the model is based on assumption and some parameters of the model are hard to find. There should be some improvement to the model or find missing parameters in future; we do expect better results from the model. Therefore, the study calls or is open to other researchers to get in the field for refining the study.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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