International Journal of Scientific Engineering and Applied Science (IJSEAS) – Volume-6, Issue-6, June 2020
ISSN: 2395-3470
www.ijseas.com

Mathematical Modelling Of the Effect OF HIV/AIDS on Sickle Cell Genotype.

I. C. ELI[1] and K. W. BUNONYO[2]

Department of Mathematics and Statistics, Federal University Otuoke, Yenagoa, Nigeria.

Abstract:

With the help of mathematical modelling a system of ODE's involving sickle cell, HIV and T-cells are formulated. Using characteristic equation, the eigen values are obtained to test for the steady state solution. Finally, simulations were carried out to provide the real-life answers.

Keywords: Ordinary differential equations, sickle cells, HIV, T-cell, eigen values and matlab.

1. Introduction:

Most times when real life situation is modeled and analyzed, it usually leads to ordinary differential equation [1]. The spread of HIV is also associated strongly with the spatial distribution of high risk groups. The distribution of AIDS cases do not just varies by cities and states but also by geographical regions [2]. Though, blood group antigens have been reported many times to be associated with many disease condition [3,4,]. Studies have shown that ABO blood groups have an impact on immunity to infection in individuals having a particular blood group because of its associations observed when investigated [5,6,7,8]. The ABO blood group system which was first discovered by Landstemer in 1901 [9-11] is thus, one of the series of glycoproteins and glycolipids present on the human red cells which constitute the red cell antigen. The Rh was later discovered by Landstemer and Weiner in 1941 [12]. These antigens which are genetically controlled are inherited in Mendolian till death [11]. About 700 erythocyte antigens have been described and organized into 30 blood transfusion out of which ABO and Rh

are the most important [10]. Blood group antigens plays an important role in transfusion safely, understanding genetics, inheritance pattern, as well as solving certain medico-legal, issues [13]. In this modern age of medicine besides their importance in evolution, their relation to disease and environment is increasingly imperative. Some blood groups can act as a receptor and ligand for bacteria, parasites and viruses. Pathologically, certain blood groups have been associated with diseases. For instance, blood group A individual are known to be more susceptible to coronary heart disease (CHD), it also have higher level of low density lipoprotein (LDL) compared to other blood groups [14]. In this paper, we consider the Mathematical modelling of the effect of HIV/AIDS on sickle cell Genotype.

2. Mathematical Formulation

In this section, we would develop a mathematical model to study the dynamic interaction between Sickle cells and HIV infected cells with the constant supply of the active T cells from the thymus. However, before we delve into the development of the mathematical models, lets us consider the compartment diagram showing their relationship.

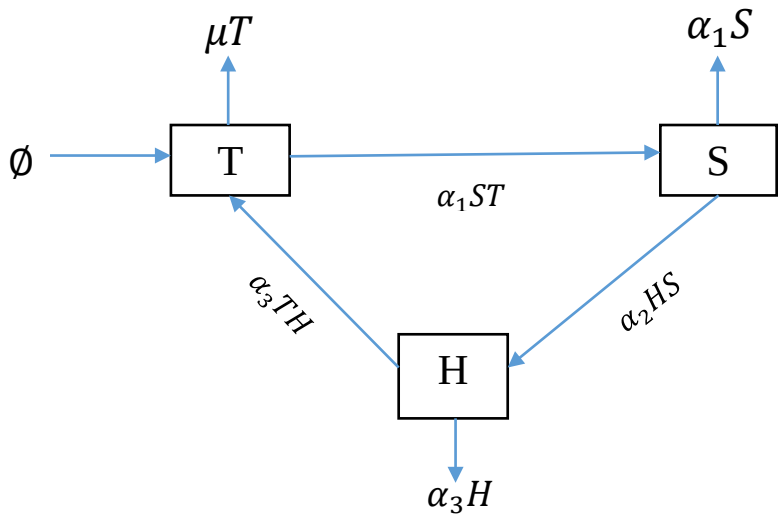


Figure 1: Compartment diagram showing the relationship between Sickle cell and HIV infected cell with constant flux of T cells

In view of the compartment diagram as shown above, we consider the following assumptions:

1. There is constant supply of T cells from the thymus to keep the immune system afloat
2. The thymus only strengthen the Sickle cells
3. The interaction between Sickle cell with infected HIV cell leads to the death of Sickle cell

2.1 Definition of Terms:

We may define the parameters that are involved in the compartment diagram (See Fig 1), they are as follows:

φ = T cells influx from the thymus

S = Sickle cell population

H = HIV infected cell population

μ = Death rate of T cells

Using the compartment model in Fig 1 with the above assumptions, we have the following models for T cells, Sickle cells and HIV infected cells respectively as:

$$\frac{dT}{dt} = \phi - \mu T - \alpha_1 TH \tag{1.1}$$

$$\frac{dS}{dt} = -\mu S - \alpha_2 HS \tag{1.2}$$

$$\frac{dT}{dt} = -\mu H + \alpha_1 TH - \alpha_2 HS \qquad (1.3)$$

2.2 Determination of Steady State Solutions:

Here, we determine the steady state solutions of equations (1.1) – (1.3). At steady state:

$$\frac{dT}{dt}, \frac{dS}{dt} \; and \; \frac{dH}{dt} = 0 \qquad (1.4)$$

Considering equation (1.4) on equations (1.1) – (1.3), we have the following representations:

$$\phi - \mu T_0 - \alpha_1 T_0 H_0 = 0 \qquad (1.5)$$

$$-\mu S_0 + \alpha_2 H_0 S_0 = 0 \qquad (1.6)$$

$$-\mu H_0 + \alpha_1 T_0 H_0 - \alpha_2 H_0 S_0 = 0 \qquad (1.7)$$

But at the steady state solutions, T$\rightarrow T_0$, S$\rightarrow S_0$, H$\rightarrow H_0$, then equations (1.5) – (1.7) can be transform as follows:

$$\phi - \mu T_0 - \alpha_1 T_0 H_0 = 0 \qquad (1.8)$$

$$-\mu S_0 + \alpha_2 H_0 S_0 = 0 \qquad (1.9)$$

$$-\mu H_0 + \alpha_1 T_0 H_0 - \alpha_2 H_0 S_0 = 0 \qquad (1.10)$$

Equations (1.8) – (1.10) for the trivial steady state solutions, we obtain the following:

$$S_0(-\alpha_1 - \alpha_2 H_0) = 0 \qquad (1.11)$$

Such that $S_0 = 0, (-\alpha_1 - \alpha_2 H_0) \neq 0$ similarly

$(-\mu - \alpha_1 T_0)H_0 = 0$ (1.12)

Such that $H_0 = 0, (-\mu - \alpha_1 T_0) \neq 0$ (1.13)

Substitute the values of $S_0 = H_0 = 0$ into equation (1.7) ,we obtain the following:

$T_0 = \frac{\phi}{\mu}$ (1.14)

Thus the trivial steady state solutions are:

$\left(T_0, S_0, H_0\right) = \left(\frac{\phi}{\mu}, 0,0\right)$ (1.15)

We can now solve for the non-trivial steady state solution involving Sickle cell and HIV cells by letting the steady state solutions, T→T_1, S→S_1, H→ H_1, then equations (1.8) – (1.10) at steady state becomes:

$\phi - \mu T_1 - \alpha_1 T_1 H_1 = 0$ (1.16)

$-\mu S_1 + \alpha_2 H_1 S_1 = 0$ (1.17)

$-\mu H_1 + \alpha_1 T_1 H_1 - \alpha_2 H_1 S_1 = 0$ (1.18)

We solve for the non-trivial steady state solutions in equations (1.16) – (1.18) as:

From equation (1.17), we have:

$S_1(-\mu + \alpha_2 H_1) = 0$ So that $S_1 \neq 0$ similarly

$(-\mu + \alpha_2 H_1) = 0$, so that $H_1 = \frac{\mu}{\alpha_2}$ (1.19)

In similar vein, from equation (1.10) we could recall as:

$T_1 = \frac{\phi}{(\mu + \alpha_1 H_1)}$ (1.20)

If we substitute the value of $H_1 = \frac{\mu}{\alpha_2}$ in (1.14), we have can simplify (1.20) as follows;

$$T_1 = \frac{\phi}{\left(\mu + \frac{\alpha_1 \mu}{\alpha_2}\right)} \tag{1.21}$$

From equation (1.18), we substitute the value of H_1 and equation (1.21) into equation (1.18) and resolve as:

$$S_1 = \frac{\alpha_1 \mu \phi \left(\frac{\mu^2}{\alpha_2}\right)}{\left(\mu + \frac{\alpha_1 \mu}{\alpha_2}\right)\left(\frac{\alpha_2^2 \mu}{\alpha_2}\right)} \tag{1.22}$$

2.3 Linearization of the System

In order to obtain different Eigen values to check for the stability of the system, we carryout linearization of the system by the letting the functions, F_1, F_2, F_3, to represent equations (1.1) – (1.3) respectively as follows:

$$F_1 = \phi - \mu T_0 - \alpha_1 T_0 H_0 = 0 \tag{1.23}$$

$$F_2 = -\mu S_0 + \alpha_2 H_0 S_0 = 0 \tag{1.24}$$

$$F_3 = -\mu H_0 + \alpha_1 T_0 H_0 - \alpha_2 H_0 S_0 = 0 \tag{1.25}$$

We differentiate equations (1.11) – (1.13) partially with respect to the cell populations, that is, T, H, S, as follows:

$$J_{11} = \left.\frac{\partial F_1}{\partial T}\right|_{(T_0, S_0, H_0)} = -\mu - \alpha_1 H_0$$
$$J_{12} = \left.\frac{\partial F_1}{\partial S}\right|_{(T_0, S_0, H_0)} = 0$$
$$J_{13} = \left.\frac{\partial F_1}{\partial H}\right|_{(T_0, S_0, H_0)} = \alpha_1 T_0 \tag{1.26}$$

$$J_{21} = \left.\frac{\partial F_2}{\partial T}\right|_{(T_0,S_0,H_0)} = 0$$

$$J_{22} = \left.\frac{\partial F_2}{\partial S}\right|_{(T_0,S_0,H_0)} = -\mu + \alpha_2 H_0$$

$$J_{23} = \left.\frac{\partial F_2}{\partial H}\right|_{(T_0,S_0,H_0)} = \alpha_2 S_0 \qquad (1.27)$$

$$J_{31} = \left.\frac{\partial F_3}{\partial T}\right|_{(T_0,S_0,H_0)} = \alpha_1 H_0$$

$$J_{32} = \left.\frac{\partial F_3}{\partial S}\right|_{(T_0,S_0,H_0)} = -\alpha_2 H_0$$

$$J_{33} = \left.\frac{\partial F_3}{\partial H}\right|_{(T_0,S_0,H_0)} = -\mu + \alpha_1 T_0 - \alpha_2 S_0 \qquad (1.28)$$

We can formulate a Jacobian Matrix using equations (1.26) – (1.28) as follows:

$$\begin{pmatrix} J_{11} & J_{12} & J_{13} \\ J_{21} & J_{22} & J_{23} \\ J_{31} & J_{32} & J_{33} \end{pmatrix} \qquad (1.29)$$

We can substitute the trivial steady state solutions into equation (1.29) we have:

$$\begin{pmatrix} (-\mu - \alpha_1 H_0) & 0 & \alpha_1 T_0 \\ 0 & (-\mu + \alpha_2 H_0) & \alpha_2 S_0 \\ \alpha_1 H_0 & -\alpha_2 H_0 & (-\mu + \alpha_1 T_0 - \alpha_2 S_0) \end{pmatrix} \qquad (1.30)$$

In the same vein, we can now do the linearization for the non-trivial steady state solutions as follows:

$$J_{11} = \left.\frac{\partial F_1}{\partial T}\right|_{(T_0,S_0,H_0)} = -\mu - \alpha_1 H_1$$
$$J_{12} = \left.\frac{\partial F_1}{\partial S}\right|_{(T_0,S_0,H_0)} = 0$$
$$J_{13} = \left.\frac{\partial F_1}{\partial H}\right|_{(T_0,S_0,H_0)} = \alpha_1 T_1 \quad (1.31)$$

$$J_{21} = \left.\frac{\partial F_2}{\partial T}\right|_{(T_0,S_0,H_0)} = 0$$
$$J_{22} = \left.\frac{\partial F_2}{\partial S}\right|_{(T_0,S_0,H_0)} = -\mu + \alpha_2 H_1$$
$$J_{23} = \left.\frac{\partial F_2}{\partial H}\right|_{(T_0,S_0,H_0)} = \alpha_1 S_1 \quad (1.32)$$

$$J_{31} = \left.\frac{\partial F_3}{\partial T}\right|_{(T_0,S_0,H_0)} = \alpha_1 H_1$$
$$J_{32} = \left.\frac{\partial F_3}{\partial S}\right|_{(T_0,S_0,H_0)} = -\alpha_2 H_1$$
$$J_{33} = \left.\frac{\partial F_3}{\partial H}\right|_{(T_0,S_0,H_0)} = -\mu + \alpha_1 T_1 - \alpha_2 S_1 \quad (1.33)$$

We can formulate a Jacobian Matrix using equations (1.31) – (1.33) as follows:

$$\begin{pmatrix} J_{11} & J_{12} & J_{13} \\ J_{21} & J_{22} & J_{23} \\ J_{31} & J_{32} & J_{33} \end{pmatrix} \quad (1.34)$$

We can substitute the trivial steady state solutions into equation (1.34) we have:

$$\begin{pmatrix} (-\mu - \alpha_1 H_1) & 0 & \alpha_1 T_1 \\ 0 & (-\mu + \alpha_2 H_1) & \alpha_2 S_1 \\ \alpha_1 H_1 & -\alpha_2 H_1 & (-\mu + \alpha_1 T_1 - \alpha_2 S_1) \end{pmatrix} \quad (1.35)$$

2.4 Characteristics Equations

We formulate the characteristics equation so as to obtain the different Eigen values for the trivial steady state and non-trivial steady state solutions as follows

$$\left|J-\lambda I\right|=\left|\begin{pmatrix}(-\mu-\alpha_1 H_0) & 0 & \alpha_1 T_0\\ 0 & (-\mu+\alpha_2 H_0) & \alpha_2 S_0\\ \alpha_1 H_0 & -\alpha_2 H_0 & (-\mu+\alpha_1 T_0-\alpha_2 S_0)\end{pmatrix}-\begin{pmatrix}\lambda & 0 & 0\\ 0 & \lambda & 0\\ 0 & 0 & \lambda\end{pmatrix}\right|=0 \quad (1.36)$$

And that of non-trivial steady state solutions as:

$$\left|J-\lambda I\right|=\left|\begin{pmatrix}(-\mu-\alpha_1 H_1) & 0 & \alpha_1 T_1\\ 0 & (-\mu+\alpha_2 H_1) & \alpha_2 S_1\\ \alpha_1 H_1 & -\alpha_2 H_1 & (-\mu+\alpha_1 T_1-\alpha_2 S_1)\end{pmatrix}-\begin{pmatrix}\lambda & 0 & 0\\ 0 & \lambda & 0\\ 0 & 0 & \lambda\end{pmatrix}\right|=0 \quad (1.37)$$

Where $I=\begin{pmatrix}1 & 0 & 0\\ 0 & 1 & 0\\ 0 & 0 & 1\end{pmatrix}$

We can now insert the value of T_0, S_0, H_0 in (1.36), we have;

$$\begin{pmatrix}-\mu-\lambda & 0 & \alpha_1\dfrac{\phi}{\mu}\\ 0 & -\mu-\lambda & 0\\ 0 & 0 & -\mu+\dfrac{\phi}{\mu}-\lambda\end{pmatrix} \quad (1.38)$$

We obtain the Eigen values for the trivial steady state as;

$$\left.\begin{aligned}\lambda_1 &= -\mu \\ \lambda_2 &= -\mu \\ \lambda_3 &= -\mu + \frac{\phi}{\mu}\end{aligned}\right\} \tag{1.39}$$

We can now insert the value of T_0, S_0, H_0 in (1.37), we have;

$$\begin{pmatrix} -\mu - \frac{\alpha_1\mu}{\alpha_2} - \lambda & 0 & \frac{\alpha_1\phi}{\left(-\mu + \frac{\alpha_1\mu}{\alpha_2}\right)} \\ 0 & -\mu - \frac{\alpha_2\mu}{\alpha_2} - \lambda & \frac{\alpha_2\alpha_1\mu\phi\left(\frac{\mu^2}{\alpha_2}\right)}{\left(-\mu + \frac{\alpha_1\mu}{\alpha_2}\right)\left(\frac{\alpha_2^2\mu}{\alpha_2}\right)} \\ \frac{\alpha_1\mu}{\alpha_2} & -\frac{\alpha_2\mu}{\alpha_2} & -\mu + \frac{\alpha_1\phi}{\left(-\mu + \frac{\alpha_1\mu}{\alpha_2}\right)} - \frac{\alpha_2\alpha_1\mu\phi\left(\frac{\mu^2}{\alpha_2}\right)}{\left(-\mu + \frac{\alpha_1\mu}{\alpha_2}\right)\left(\frac{\alpha_2^2\mu}{\alpha_2}\right)} - \lambda \end{pmatrix} \tag{1.40}$$

We obtain the Eigen values for the non trivial steady state as

$$\left.\begin{aligned}\lambda_1 &= -\mu - \frac{\alpha_1\mu}{\alpha_2} \\ \lambda_2 &= -\mu - \frac{\alpha_2\mu}{\alpha_2} \\ \lambda_3 &= -\mu + \frac{\alpha_1\phi}{\left(-\mu + \frac{\alpha_1\mu}{\alpha_2}\right)} - \frac{\alpha_2\alpha_1\mu\phi\left(\frac{\mu^2}{\alpha_2}\right)}{\left(-\mu + \frac{\alpha_1\mu}{\alpha_2}\right)\left(\frac{\alpha_2^2\mu}{\alpha_2}\right)}\end{aligned}\right\} \tag{1.41}$$

3 Result

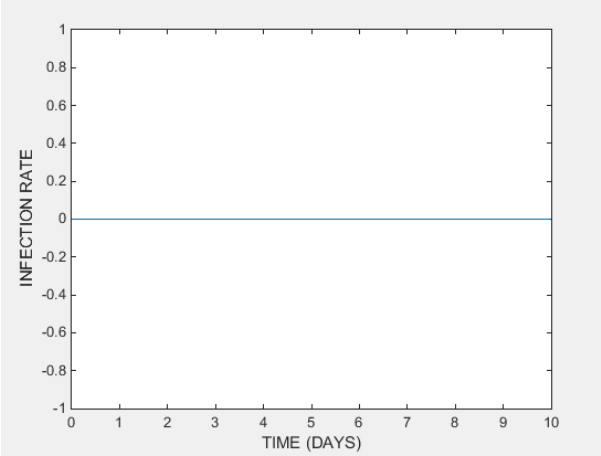
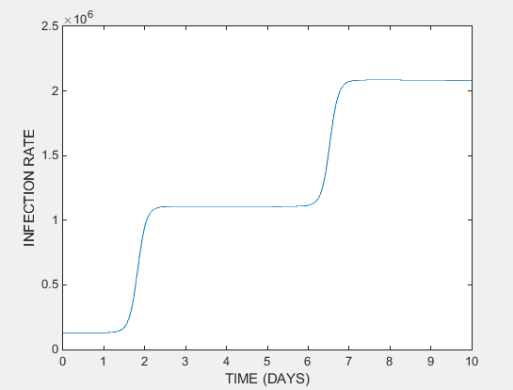


Figure 2: trivial steady state models. The disease-free model showing the infection rate of the Virus with respect to time after ten days.

The disease-free model shows no growth of virus infection giving a steady rate with respect to time as shown in figure 1. This shows that at the trivial steady state model is steady.



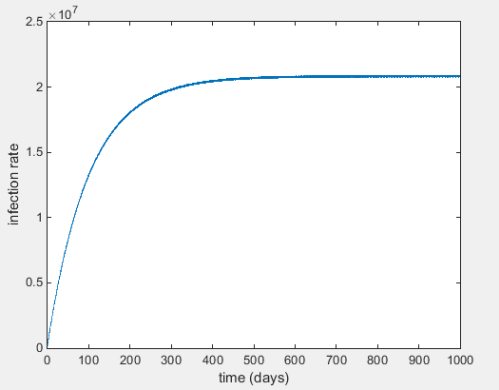


Figure 3: non trivial steady state model. The model showing the infection rate of the virus with respect to time after ten days and after a thousand days of viral infection,

From figure 2, we observe that there is an exponential rate of infection increase but also shows that the model is stable after a period of time. It shows stability and then rapid growth, going back to being stable. This shows that at the initial point of infection there is a sufficient attempt to clear the virus from the blood by the T cells.

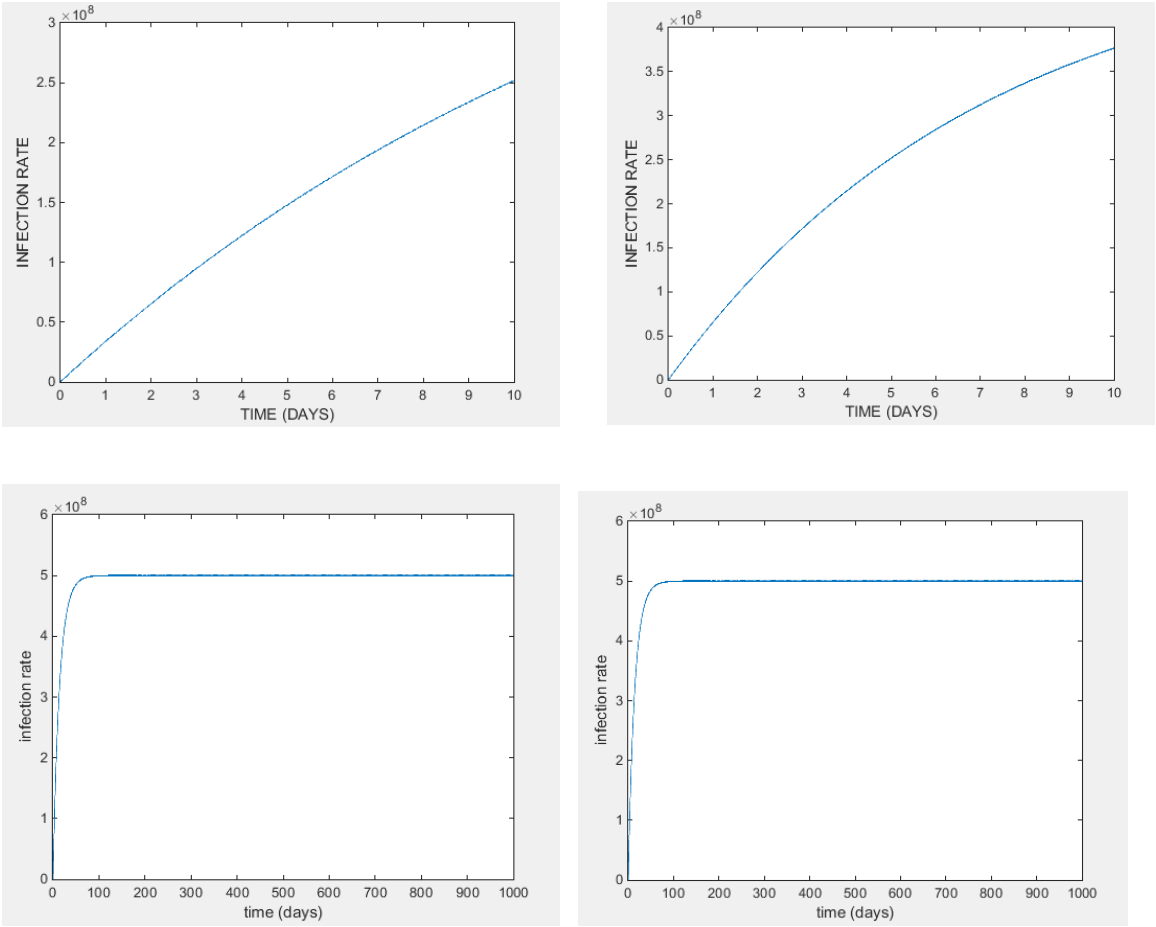


Figure 4: Non trivial steady state model. The model showing the infection rate of the virus with respect to time after ten days and after a thousand days of viral infection after increase in production of CD4+ T cells and rate of cell infection

After increasing the number of productions of CD4+ T cells there was a linear growth of viral load before the steady state. This shows that the non-trivial steady state model is steady.

The non-trivial steady state shows rapid increase in virus infection rate with respect to time. The growth of the virus since the values of the viral load increased drastically, it would seem portion of the virus is produced each day. There is an explanation for the high viral loads in the presence of CD4+ T cells count. The inability of the body to efficiently clear the infection. Thus, it is reasonable to hypothesize that as HIV infection progress to AIDS, the immune system loses the ability to clear virus effectively, resulting to a long residue time for the virus population

4. DISCUSSION

The more supply of CD4+ T cells to the blood steam causes the increase in infection due to the inability of the T cells to clear the virus, therefore being infected by the virus and increasing the multiplication of the viral load. Another explanation is that there are other viral reservoirs that become larger and larger or more active as the T cells are lost to the virus infection progressing to AIDS.

Research indicates that early in infection, CD4þ T cells account for more than 90% of the productively infected cells in the body (Haase, 1999). If CD4þ T cells remain the main source of virus throughout the course of infection, then the relationship between the immune system and the virus must change. It is possible that an HIV weakened immune system may lose the ability to clear virus efficiently, as it does with many types of pathogens (Hansen et al., 1985; Barr, 1992; Matsuo et al., 2001). Though some studies suggest that clearance rates do not change throughout infection (Ho et al., 1995), there is a significant amount of variation in the measurements derived from different studies (Ho et al., 1995; Mittler et al., 1999; Ramratnam et al., 1999).

5. CONCLUSION

There is no significant relationship between the genotype of a patient and the growth of the HIV. The more production of CD4+ T cells the more effective the virus becomes and the more the patient becomes more susceptible to the infection.

References

[1] Burden, R. L. and Faires, J. D. (2011). Numerical analysis, Ninth edition, Canada.

[2] Lange, F. R, Snyder, Lozovsky D, Kaistha V, Kaczaniuk M. A, and Jaffe J. H, (1988). Geographic distribution of human immune deficiency virus markers in parenteral drug abusers. AMJ Public Health 78, pp446.

[3] Kassim O, Ejezie G. ABO blood groups in Malaria and Schistosomiasis haematobium. Acta Trop …. 1982; 39.179-84.

[4] Tursen U, Tiffik E, Unal S, Gunduz O, Kaya T1, et al. Relationship between ABO blood groups and skin cancers Dermatol. On line J, 2005:11:pp44.

[5] Opera K. Onchocerciasis and ABO blood group status: a field based study. Int. J Trop. Med, 2007: 2(4):123-125.

[6] Abdulazeez A, Alo E, Rebecca S. Carriage rate of Human Immuno Deficiency Virus (HIV) infection among different ABO and Rhesus blood groups in Adamawa State, Nigeria. Biomed Res.., f2008:19:pp41-44.

[7] Ndambaa J, Gomoa E, Nyazemab N, Makazaa N, relations to the ABO blood groups among school children in Zimbabwe. Acta Trop., 1997;65. Pp181-190.

[8] Blackwell cc, Dundas S, James vs, Mackenzie Ac, Braun JM, et al. Blood group and susceptibility to disease caused by Eschetichia coli 0 157. J. Infect. Dis; 2002, 185 (3): 393-396.

[9] Garraty G. Dzik W, Issitt P. Lubin D, Reid M, et al. Terminology for blood group antigens and genes-historical origin and guideline in the new millennium. Transfusion, 2000, 40:477-489.

[10] Rahman M, Lodlu Y. Frequency of ABO and Rhesus blood groups in blood donors in Punjab Pak J. Med. Sci, 2004;20: 315-318.

[11] Lease M, Bazuaye G. Distribution of ABO and Rh-D blood groups in the Benin area of Niger-Delta: Implication for regional blood transfusion. Asian J. Transfus, Sci., 2008; 2(1):3-5.

[12] Ahmad J, Taj A, Rahim A, Shah A, Rheman M. frequency of Hepatitis B and Hepatitis C in health blood donors of NWFP: a single centre experience J. post grad Med. Inst, 2004; 18(3): 343-352.

[13] Wazirali H, Ashfane RA Herzig JW. Association of blood group A with increased risk of coronary heart disease in the Pakistan population. Pak J. Physiol, 2005; 1:(1-2):1-3