

CHAPTER 1

INTRODUCTION

This chapter gives a brief explanation of the fundamental aspects of HIV/AIDS. The chapter also explains the basic terms and terminologies used in the thesis and gives a brief discussion of the same.

1.1 HIV/AIDS, AN INTRODUCTION

HIV/AIDS stands for Human Immunodeficiency Virus / Acquired Immune Deficiency (or immunodeficiency) Syndrome. Immunodeficiency refers to any deficiency in the immune response. The deficiency could be inherited or acquired. Human Immunodeficiency Virus (HIV) refers to a class of virus called retroviruses (a virus that has RNA as genetic material instead of DNA) and the disease it causes, one of the deadliest disease of modern times, is called the Acquired Immunodeficiency Syndrome (AIDS)(UNAIDS, 2018c). AIDS is a severe phase of HIV infection. AIDS is a result of a damaged immune system caused due toinfection of HIV, resulting in an increasing number of severe illnesses. These illnesses, are opportunistic illnesses, in which disease-causing agents take the opportunity of a weak immune system and prey on the body and harm the vital organs. Thus AIDS results in a spectrum of disease conditions in an individual.

1.1.1 World Scenario

AIDS is one of the greatest public health challenges of the 20th century since its discovery in early 80's (Mills, Kanters and Ford, 2017). According to the Joint United Program on HIV/AIDS (UNAIDS) statistics, at the end of 2017, 36.9 million people globally live with HIV/AIDS (UNAIDS, 2018a). UNAIDS strategizes making 2030 as the year to end the AIDS epidemic (UNAIDS, 2015) which is almost a decade away.

1.1.2 Indian Scenario

India is not away from the HIV/AIDS epidemic. India has a large and evolving HIV epidemic (Biggar *et al.*, 2009) and India has the second-largest number of HIV/AIDS patients in the world (Dhir, 2008). According to UNAIDS statistics, at the end of 2017, 2.1 million people in India lived with HIV/AIDS (UNAIDS, 2018b). As per the 2015 HIV Estimation report, the adult (15–49 years) HIV prevalence was estimated at 0.26% (Male-0.30% and Female-0.22%) in 2015 in India. The numbers have shown a steady decline from an estimated peak of 0.38% in 2001-03 through 0.34% in 2007 to 0.26% in 2015. Among the States/UTs, in 2015, Manipur has shown the highest estimated adult HIV prevalence (1.15%) and least being Himachal Pradesh (0.07%).

The incidences of HIV / 1000 population for various parts of India is shown in Figure 1.1(NACO_&_ICMR, 2017). According to the figure, on an average 0.07 people of 1000 population are positive for HIV. While Himachal Pradesh has the least HIV instances with 0.01/1000, Mizoram has the highest of 1.32 / 1000.

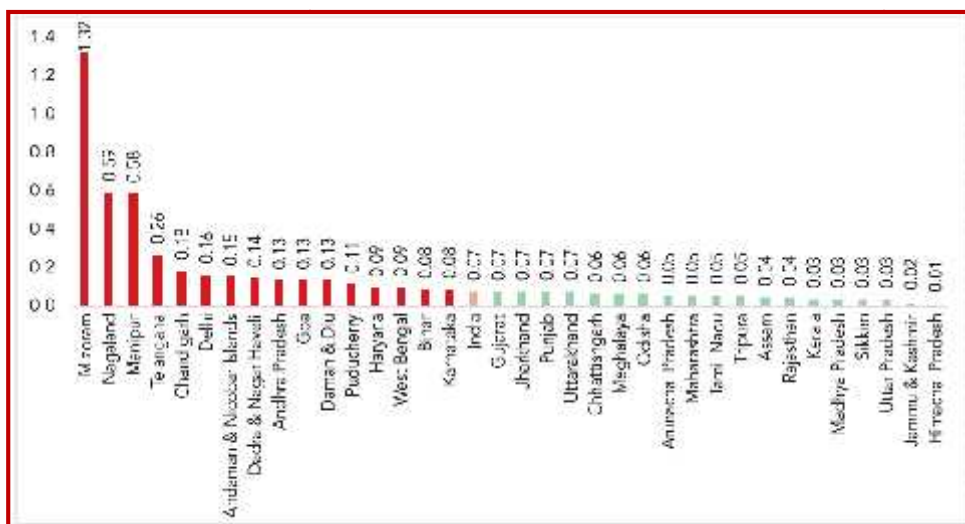


Figure 1.1: HIV Incidences / 1000 population in various parts of India

Another estimate by NACO, Government of India shows that the total number of people living with HIV (PLHIV) in India was 21.17 lakhs in 2015. Children (< 15 years) accounted for 6.54%, while women contributed around 40.5% of total HIV infections. Undivided Andhra Pradesh and Telangana have the highest estimated number of PLHIV (3.95 lakhs). Figure 1.2 shows the estimated number of PLHIV in 2015. The estimated number of new HIV infections in 2015 was approximately 86,000(NACO, 2018).

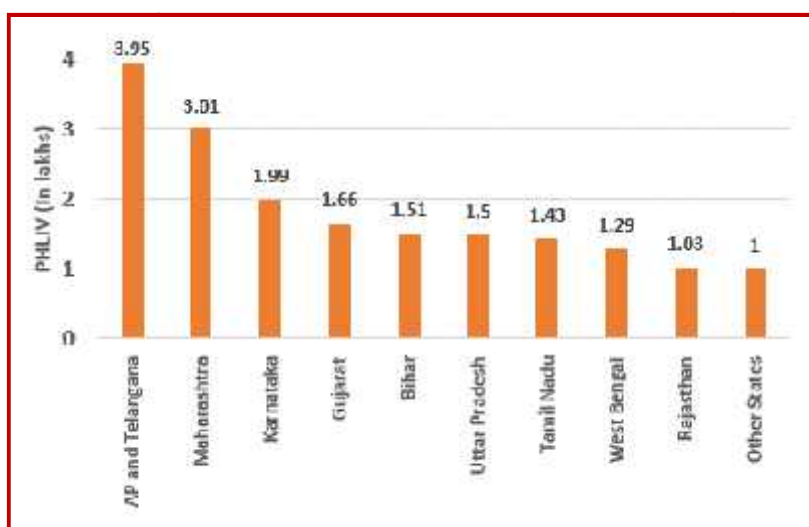


Figure 1.2: Estimated number of PLHIV in various states of India

1.2 IMMUNE SYSTEM AND IMMUNE PARAMETERS IN HIV/AIDS

The human body is persistently attacked by disease-causing agents, the pathogens. The pathogens could be viruses, bacteria, fungi, protozoa or worms. However, the pathogens would not be able to harm the body since the body has a system to fight against the pathogens through the immune system. The immune system provides two types of immunity; innate immunity and adaptive (acquired) immunity.

The innate immunity comprising of several cellular components viz., neutrophils, eosinophils, basophils, mast cells, monocytes, macrophages, dendritic cells and natural killer (NK) cells provide built-in (available from birth), quick, non-specific protection against pathogens. Acquired immunity comprising of two major varieties of lymphocytes; the T-

cells and the B-cells provides a relatively slower response, specific immunity to the type of pathogen.

T-cells assist other cells in immune response, limit excessive or undesired immune response and kills cells infected with pathogens. B-cells produce antibodies, also providing immunity.

Of the different types of lymphocytes, helper T cells that activate the other types of lymphocytes are the ones attacked by HIV. HIV by infecting these cells targets the first step in the initiation of an adaptive immune response. Some findings also explain that apart from T-cells, B cells are also affected during HIV infection (Moir and Fauci, 2014). Broadly, the T-cells are classified into four types, T-helper cells, T-memory cells, T-suppressor cells and T-killer cells. Of these, the important types of T-cells considered in the current research are the CD4 and CD8 cells which are also referred to as T-Helper cells and T-Killer cells respectively. The same is discussed in brief.

1.2.1 CD4 cells

CD4 (Cluster of Differentiation 4) T cells are T-Helper (T_H) cells. These cells initiate an immune response against an invading HIV. CD4 cell count provides a picture of immune system competence, with higher CD4 counts typically signifying a healthier immune system (Ahmadi *et al.*, 2001; Ampofo *et al.*, 2006).

CD4 glycoprotein on the cell surface of T cells interacts with a similar molecule (MHC II) on the surface of another kind of immune system cell called antigen-presenting cell (APC). APC's role is to engulf the pathogen, chop the protein and lipids component of the pathogen and load the same onto MHC II molecules which stand out like an antenna on the surface of APC to be recognized by T_H cells (through CD4). This interaction of CD4 and MHC II molecules sets off cytokinesculminating in the production of antibodies against the pathogen.

HIV mainly infects the CD4⁺ T cells, eventually reducing their numbers. This reduction in CD4 cells makes a person more likely to get other infections or infection-related cancers. If the CD4 cell count is <200, the person is said to have AIDS. Hence CD4 cell count is an important marker determining the extent of damage caused on the immune system by HIV (Mair *et al.*, 2008). The normal range of CD4 counts depends on time, age, gender and place. (Table 1.1)(Howard *et al.*, 1996; Uppal, Verma and Dhot, 2003; Hussain *et al.*, 2015; Simon, Hollander and Michael, 2015; Klein and Flanagan, 2016).

1.2.2 CD8 cells

CD8⁺ T cells (T_C), are cytotoxic T cells or T-killer cells, which play a prominent role in defense against intracellular pathogens like viruses and bacteria and they also perform an important role in tumor surveillance. Like CD4 on T_H, CD8 is a glycoprotein on T_C which interacts with MHC class I molecules present on almost all cell types. When T_C cells identify the infected cells (by the interaction of CD8 with MHC class I) it prepares to kill them either by producing anti-microbial cytokines like TNF and IFN or by synthesizing and releasing molecules to dissolve the infected cells' cell membrane and digest the internal structures of the infected cell. The latter method is called apoptosis. CD8 cells also stop the activity of CD4 cells when there is sufficient antibodies produced in the body(Scanlan *et al.*, 1998).

1.2.3 CD3 cells

The CD3 (cluster of differentiation 3) T cell co-receptor helps to activate both the cytotoxic T cell (CD8⁺ naive T cells) and also T helper cells (CD4⁺ naive T cells). Thus CD3 cells are the precursor for the CD4 and CD8 cells. The CD3 cells recognize the antigens and depending on the antigen it encounters it either mature into CD4 or Cd8 cells. Thus the total number of CD4 cells and CD8 cells is equal to the number of CD3 cells, given by, CD3 cells = CD4 cells + CD8 cells.

1.2.4 CD4/CD8 ratio

CD4/CD8 ratio is a key biomarker for HIV infection (Serrano-Villar and Deeks, 2015). It is the ratio of the peripheral T cells (CD4 cells) to the killer cells (CD8 cells). CD4/CD8 ratio helps in evaluating the immune system for both monitoring the immune dysfunction and viral reservoir size in immune-based clinical trials (Lu *et al.*, 2015). A low CD4/CD8 ratio has also been identified in the general population as a hallmark of immunosenescence and a surrogate of all-cause mortality (Serrano-Villar *et al.*, 2014). Low CD4/CD8 ratio indicates impairment in CD4 T cell regeneration and the persistent elevation of CD8 T cell counts, thereby indicating major T cell dysfunction (Vyboh *et al.*, no date; Serrano-Villar *et al.*, 2014). On the other hand, a higher CD4/CD8 ratio indicates suppression of viral loads allowing progressive CD4 T cell recovery paired with a persistent elevation of CD8 T cells, which also indicates that a treatment regime is working well (Lu *et al.*, 2015). It is always preferable to have more peripheral T cells to avoid infection of the body against harmful viruses. Hence the CD4/CD8 ratio should be more than one. However, the ratio depends on several factors like age, gender, health/infection status, environment and place. With specific reference to HIV, the CD4/CD8 ratio indicates the state of the infected and also indicates, the effectiveness of ART regime or other interventions.

Table 1.1: Typical values of CD3, CD4, CD8 counts and CD4/CD8 ratio

Sl.	Sample category	Mean CD3 (Range) or Mean \pm SD Cells/~L	Mean CD4 (Range) or Mean \pm SD Cells/~L	Mean CD8 (Range) or Mean \pm SD Cells/~L	Mean CD4/CD8 ratio (Range)	Reference
1	<ul style="list-style-type: none">) Healthy) Kenyans) Females 	1787 (697-2841)	1010 (422-1572)	659 (187-1180)	1.51 (0.49 – 2.64)	(Bosire <i>et al.</i> , 2013)
2	<ul style="list-style-type: none">) Healthy) Kenyans) Males 	1610 (581-2641)	889 (320-1459)	644 (185-1140)	1.69 (0.55-2.95)	(Bosire <i>et al.</i> , 2013)

Sl.	Sample category	Mean CD3 (Range) or Mean \pm SD Cells/ \sim L	Mean CD4 (Range) or Mean \pm SD Cells/ \sim L	Mean CD8 (Range) or Mean \pm SD Cells/ \sim L	Mean CD4/CD8 ratio (Range)	Reference
3	<ul style="list-style-type: none">)} Healthy)} Kenyans)} Males and Females)} 16-19 years 	1603	912	611	1.70	(Bosire <i>et al.</i> , 2013)
4	<ul style="list-style-type: none">)} Healthy)} Kenyans)} Males and females)} 20-30 years 	1641	898	641	1.54	(Bosire <i>et al.</i> , 2013)
5	<ul style="list-style-type: none">)} Healthy Kenyans – General population in age group 31-55 years 	1742	997	693	1.54	(Bosire <i>et al.</i> , 2013)
6	<ul style="list-style-type: none">)} Normal)} Indians)} Adults 	1490 \pm 469	799 \pm 282	607 \pm 210	1.39 \pm 0.45	(Hussain <i>et al.</i> , 2015)
7	<ul style="list-style-type: none">)} Normal)} Indians)} Children 	2249 \pm 731	1102 \pm 436	1003 \pm 477	1.32 \pm 0.71	(Hussain <i>et al.</i> , 2015)
8	<ul style="list-style-type: none">)} HIV-Positive)} Early infection)} Indians)} Adults 	1658 \pm 807	703 \pm 470	958 \pm 363	0.72 \pm 0.34	(Hussain <i>et al.</i> , 2015)
9	<ul style="list-style-type: none">)} HIV-Positive)} Full-blown AIDS)} Indians)} Adults 	1665 \pm 1061	283 \pm 249	1188 \pm 622	0.22 \pm 0.13	(Hussain <i>et al.</i> , 2015)
10	<ul style="list-style-type: none">)} HIV-Negative)} Sengalese)} General 	1471 \pm 540	870 \pm 347	514 \pm 260	1.90 \pm 0.77	(Mair <i>et al.</i> , 2008)
11	<ul style="list-style-type: none">)} Healthy)} Indians)} Adults)} Females)} 18-74 years 	-	963	530	1.92	(Uppal, Verma and Dhot, 2003)
12	<ul style="list-style-type: none">)} Healthy)} Indians)} Adults)} Males)} 20-68 years 	-	802	568	1.55	(Uppal, Verma and Dhot, 2003)

1.2.5 Viral load

Once HIV infects a person, the virus starts multiplying. 'Viral load' is the quantification of the virus, which is generally expressed as the number of viruses per microliter (μL) of blood.

1.3 MODES OF TRANSFER/RISK FACTORS OF HIV & PREVENTION

There are four commonly known modes of transfer/risk factors of HIV and possible options for prevention.

- J **Sexual transmission:** This is known to be the most common cause. Infection happens when there is a transfer of sexual secretions from the infected person to the non-infected one. This can be prevented by protected sex.
- J **Infected invasions:** Use of syringes and other invasive tools that were contaminated with the blood of the infected. Suitable measures to sterilize the syringes or by proper sterilization, this can be avoided.
- J **Mother to Child Transmission (MTCT):** Also called perinatal transmission or vertical transmission, which happens from infected mother to child. Vertical transmission might be during pregnancy, delivery or breastfeeding. It is said that through effective treatment and planning, MTCT can be prevented. Bottle feeding is considered to be an easy option to prevent transmission through breastfeeding in case the mother is infected.
- J **Blood transfusion:** During blood donation, in case the blood received by the person who needs blood is from an HIV infected person, it becomes a risk factor. Taking proper care in the blood banks to detect infected blood is the option to avoid such cases.

The most commonly used strategy for preventing HIV/AIDS is the "A-B-C; Abstinence, Being faithful and use Condoms". Appropriate education towards prevention is a promising option for the prevention of the spread.

1.4 CHALLENGES FACED BY HIV POSITIVE INDIVIDUALS

No effective cure currently exists, but with proper medical care, HIV can be controlled. The medicine used to treat HIV is called antiretroviral therapy or ART. If taken the right way, every day, the medicine is known to dramatically prolong the lives of many individuals infected with HIV, keep them healthy and greatly lower their chance of infecting others. Before the introduction of ART in the mid-1990s, individuals with HIV could progress to AIDS in just a few years. Today, someone diagnosed with HIV and treated before the disease is far advanced can live nearly as long as someone who does not have HIV. However, an HIV positive individual faces a number of challenges to be on par with peers who are not HIV positive. This section discusses some of the challenges faced, as applicable to the current research.

1.4.1 Quality of Life

Quality of Life (QOL) is a concept used in trying to determine how an individual functions in a society in a normally desirable manner. The quality of life attributes differ between different target groups and situations/status in life and health. Health-Related Quality of Life (HRQOL) refers to the physical, functional, social and emotional well-being of an individual. HIV+ individuals have issues regarding the quality of life (Verma, Kamble and Krishnan, 2018). With reference to children, the component could also specifically include schooling attributes. In diseased conditions where the individual/group is vulnerable to fatigue, the term Fatigue Related Quality of Life (FRQOL) is also used. The assessment of the quality of life is especially important in individuals who are not healthy. Researchers across the globe have developed several instruments to assess the quality of life for different target groups and different disease conditions. Such assessments would help develop strategies to improve the quality of life. Individuals with HIV/AIDS are known to have major issues with quality of

life(Reis *et al.*, 2011). In this background, an attempt is made to ascertain the quality of life in candidates with HIV/AIDS and how yoga could help such candidates.

1.4.2 Depression

Depression refers to the medical situation which negatively affects what an individual feel, think and act. This situation affects several facets of life hindering the activities. It affects sleep, health, education and relationships and all other activities. As it is well understood, the HIV infection renders the person weak and is prone to attacks by a variety of diseases, making the persons physically weak. Further, in view of social stigma and social rejection in HIV individual contributes to their anxiety and depression. Thus depression is more a problem in HIVs, which requires to be addressed.

1.4.3 Cognitive Functions

Cognitive functions refer to the functioning of the brain enabling an individual to acquire information, respond to the situation, attain knowledge, analyze and take decisions. It encompasses attributes such as memory, reasoning, attention, information attainment and processing. While the cognitive functions have several attributes, two of the important attributes are the psychomotor performance and executive functions. The psychomotor performance majorly refers to the speed of processing information. The executive functions refer to those functions where memory and retrieval of information from memory are required for information processing. It is reported that perinatal HIV infection results in impairment of cognitive functions among children(Ezeamama *et al.*, 2016; Nichols *et al.*, 2016; Yadav *et al.*, 2018)

1.5 NEED FOR AN INTEGRATED APPROACH

According to Luc Montagnier, who shared the Nobel Prize for co-inventing the HIV (in 2008), “HIV is just like any other passerby virus. Our body can be exposed to the virus any

number of times. If one has a strong immune system, the body can defeat the virus in a matter of weeks” (Montagnier, 2009). Although Montagnier opines that the immune system can take over HIV on its own (Montagnier, 2011), the world over 18.2 million people are on antiretroviral therapy as of June 2016 and globally 35 million people have died of AIDS-related illnesses (UNAIDS, 2018c). Further it is well known and well accepted that antiretroviral therapy has a battery of common and severe side effects (Jain, 2007; Al-Dakkak *et al.*, 2013; Margolis *et al.*, 2014; Stolbach *et al.*, 2015; Delicio, Lajos, Amaral, Cavichioli, *et al.*, 2018; Delicio, Lajos, Amaral, Lopes, *et al.*, 2018).

With no medicine as on date available to completely cure the disease, the persons infected with HIV always have an element of general fear and a component of fear of death. The infected person would always have a notion that the disease is incurable and hence is always in a disturbed state. Further adding to this is the fear of social stigma.

As HIV/AIDS is a condition with repercussions in multiple dimensions, just addressing it from a physiological perspective will not help in addressing the needs of infected persons. Hence the problem should be attacked at an integrative multi-dimensional perspective; more so, from the lifestyle perspective promoting responsible social and ethical attitude towards life. In this background it is worth to look out for a more integrated approach; of which yogic perspective could be a promising solution; both in fighting and preventing modes.

1.6 THE YOGIC APPROACH

An integrated approach accommodating yogic and spiritual perspectives could lead to better alleviation. HIV/AIDS is also a significant social issue. That apart, an approach with a lifestyle perspective promoting responsible social and ethical attitude towards life would also be an advantage.

Earlier studies have proved that yoga helps in improving the immune system in several other diseased conditions(Field, 2016). Earlier studies also have shown improvement in the quality of life in conditions like cancer, breast cancer, neuropsychiatric disorders, arthritis, diabetes substance use disorders,etc.(Field, 2011).

1.7 INTEGRATED APPROACH OF YOGA THERAPY

A human being is not just a physical mass. As also, addressing human life or an issue of health should not be limited to the correction of the physical mass. Five levels/layers of existence of human beings are identified in the yogic and other traditional texts. These five layers of existence are the *Annamaya ko a* (the physical body), *Prāṇamaya ko a* (the prāṇic body embodying the life force), *Manomaya ko a* (the mind), *Vignanamaya ko a* (the intellect) and *nandamaya ko a* (the spiritual). This aspect/idea is traditionally referred to as the *pañcakō a* model of existence. An integrated approach towards the working/maintenance of an individual or addressing one's health should be at all these five levels. Such an integrated approach is referred to as the "Integrated Approach of Yoga Therapy" (IAYT).The practice of IAYT involves five cardinal principles, one for each ko a. The principle and the practices thereon for each of the ko as are explained in brief in the following paragraphs.

(1) *Annamaya ko a*: This ko a is enhanced by the physical relaxation of the body. This can be attained through the practices of various *śānās* giving steady and comfortable postures, *a karma kriyas* (the six cleansing techniques viz., *kapālabhīti*, *neti*, *trīṭakā*, *nauli*, *dhauti* and *basti*), deep relaxation technique (DRT), cyclic meditation, yoga *nidrā*, etc.

(2) *Prāṇamaya ko a*: This ko a can be enhanced by slowing of the breath by its taming; to help the better flow of energies through the practice of different types of *prāṇāyāmas*,

pranic energization technique (PET), etc. Further, *a karma kriyas* (especially *thekap lab tiand neti*) also help.

(3) *Manomaya ko a*: This *ko a* can be enhanced by the mastering of the mind to help calm it and thereby providing a conducive environment for channelizing the energy towards combating the disease. The various practices that help in the process are the practice of silence, deep breathing by observation of the breath, the Mind Sound Resonance Technique (MSRT), the *tr taka*, concentration and meditation, *japa* (repetition of mantras or sacred words) and *japa-japa* (constant awareness of mantras or sacred words) practices.

(4) *Vign namaya ko a*: This *ko a* can be enhanced by attitudinal changes with a purpose of understanding oneself and the true purpose of life; implemented through *sv dhy ya* (self analysis and introspection), *satsanga* (lectures and discussions for understanding the spiritual knowledge that teach the real purpose of life), deep meditation which helps tackle *karmas* and *samsk ras* (the results of past and present deep-rooted actions).

(5) *nandamaya ko a*: This *ko a* can be enhanced by trying to experience bliss in day-to-day activities and taking suitable precautions against loss of vital energy of the body through the practice of *dhy na* leading to dissolving of the self with universal energy. These principles would help both in prevention mode and ‘supporting the body to improve and combating a problem’ mode. Traditional and modern texts provide practices to enhance each of the *pa cako as* (Bhargav *et al.*, 2010; Bhavanani, 2011; Kumar and Kumar, 2017).

Table 1.2: Cardinal principles of IAYT components

Sl. No.	Component	Layer/ <i>ko as</i>	Cardinal principle of IAYT component
1	Physical	<i>Annamaya ko a</i>	Relax the body
2	<i>Pr nic</i>	<i>Pr y ma ko a</i>	Slow down the breath
3	Mental	<i>Manomaya ko a</i>	Calm down the mind
4	Intellectual	<i>Vign namaya ko a</i>	Make notional corrections
5	Spiritual	<i>nandamaya ko a</i>	Experiencing bliss in day-to-day actions

All these aspects are required to be addressed in an integrated approach. This study is an attempt for the application of IAYT on HIV positive subjects to determine the effectiveness of IAYT in improving the immune functioning and the effect of IAYT on QOL amongst HIV seropositive individuals.