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Transmission, Biochemical Manifestation and CD4+ Cell Count of HIV: A Review

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Abstract: Two genetically different related forms of human immunodefficiency virus (HIV), a human lentivirus belonging to the lentivirus family, called HIV-1 and HIV-2, have isolated from patients with AIDS. HIV can be transmitted through contaminated blood and blood products; from a mother to her offspring during pregnancy, childbirth or breast feeding; or through sexual contact. Sexual transmission remains by far the predominant mode of transmission. Vertical and blood borne transmission of HIV are highly predictable and very efficient modes. Sexual transmission of HIV, however, appears to be considerably less efficient and highly variable. During the early period after primary infection with HIV widespread of dissemination of the virus and a sharp decrease in the number of CD4+T cell count occurs. The use of CD4 cell count is an important indicator of disease severity of AIDS. The patients infected with AIDS can be attacked by various opportunistic infections such as pneumonia, *Mycobacterium avium* complex, cytomegalovirus, microsporidiosis and tuberculosis. The degree of intensity of these diseases can be indicated by measuring the level of enzyme like alkaline phosphatase, alanin aminotransferase and aspartate aminotransferase, lactate dehydrogenase and creatine phosphokinase.

Key words: HIV, transmission and biochemical parameters

INTRODUCTION

Human immunodeficiency virus (HIV) causes the AIDS (Acquired Immune Deficiency Syndrome), which is a human retrovirus that belongs to the lentivirus family. Also included in this group are feline immunodeficiency virus, simian immunodeficiency virus (SIV), visna virus of sheep and the equine infectious anemia virus. These nontransforming retroviruses have several features in common[1].

- A long incubation period followed by a slowly progressive fatal outcome.
- Tropism for hematopoietic and nervous systems
- An ability to cause immunosuppression.
- Cytopathic effects *in vitro*.

Two genetically different but related forms of HIV, called HIV-1 and HIV-2, has been isolated from patient with AIDS and also closely related viruses (SIVs) are found in many species of non-human primates[1,2]. HIV-1 is the most frequent type associated with AIDS in the United States, Europe and Central Africa, whereas HIV-2 causes a similar disease principally in West Africa[1].

Since AIDS was first described in the United States, this country has majority of this reported cases and now a day it has been reported from more than 163 countries around the world and the pool of HIV-infected person in Africa and Asia is large and expanding[1].

There are some encouraging data which suggests that rapid increase in HIV prevalence have been observed in India, Vietnam, Myanmar (Burma) and South Africa and it is predicted that South Africa will experience one of the worst epidemics in Africa. The World Health Organization (WHO) estimated that, at the end of 1997; 30.6 million people worldwide were living with HIV/AIDS of which over 90% were in developing countries, two thirds in sub-Sharan Africa. The prevalence is more in cities like the Kampala, Lusaka, Yaounde and Francistown, of the sub-Shaharan countries[3,4]. In the United States, it is currently the fourth leading cause of mortality for men between the ages of 15 to 54 years[1]. The expanding epidemic of HIV infection threatens to engulf more than 40 million persons worldwide by the year 2000[5]. United Nations estimates that AIDS will reduce Africa's overall labour force by as much as 25% by the year 2010. At the current rate, the impact on the worldwide economy is estimated to reach $ 514 billion by the year 2000[6].

From the United States, the epidemiological data suggest that the adults developing AIDS may be classified into five groups[1]:

- Homosexual or bisexual males constitute by far the largest group, accounting for 60% of the reported cases. This also includes the 5% who were intravenous drug abuser.

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- Intravenous abusers with no previous history of homosexuality compose the next largest group, which represents about 23% of all the patients. This group represents the majority of all cases among heterosexuals.
- Hemophiliacs, especially those, who received large amount of factor VIII concentrates before 1985, make up 1% of all cases.
- Recipients of blood and blood components who are not hemophiliacs but who received transfusions of HIV-infected whole or components; for example platelets, plasma account for 2% of the patients. On the contrary, organs obtained from HIV-infected donors can also transmit AIDS.
- Heterosexuals contacts members of other high-risk groups (chiefly intravenous drug abusers) constitute 6% of the patient population.

In approximately 6% of cases, risk factors cannot be determined. The pediatric population comprises 2% of all AIDS cases. The remaining 20% are hemophiliacs and others who have a history of reception of bloods or blood products before 1985[1].

Transmission of HIV: HIV can be transmitted through contaminated blood or blood products; from a mother to her offspring during pregnancy, childbirth or breast feeding; or through sexual contact. Among the transmission mode, sexual transmission remains by far the predominant mode of transmission. Vertical blood borne transmission of HIV is highly predictable and very efficient modes[1].

Blood-borne transmission: For the transmission of HIV, inoculation appears to be an efficient means that depends on size of the inoculum. Therefore, the transfusion, as it possesses large inocula, is almost infectious, whereas amount of blood on the end of a needle used for medical injections is rarely infectious[7].

Intravenous drug users (IVDU): The frequency of HIV transmission among IVDU varies place to place. Low seroprevalence rates for IVDU is observed in San Francisco and in New York in the United States and it is increasing rapidly. The rapid increase in HIV infection in the IVDU community has also documented in Edinburg, Italy and Spain[7].

In IVDU group, the risk of seropositivity among addicts is high who uses regular needle sharing. Significant differences of HIV infection have observed in the IVDU community in Blacks and Hispanics than in Whites. These racial differences reported from New York, New Jersey and San Francisco. For individual who shares needles with minority group members, the risk of information is clearly greater because of higher prevalence of infection in this group[7].

Hemophiliac or coagulation disorders: The commercial factor concentrate derived from blood such, as lyophilized factor concentrates that contains HIV is responsible for developing AIDS. It is one of the causes of transmission of HIV with commercial coagulation factor concentrates; each derived from pooled plasma of several thousand donors. It is observed that a steady increase occurred in the prevalence of HIV seropositivity in hemophiliacs from 1% in 1978 to 20% in 1980, 70% to 1984 and 90% in 1985. Uncertainty remains in the proportion of hemophiliac/coagulation disorder of HIV infected persons to develop AIDS. The relative risk has been reported higher compared to other risk groups. The aspect of the incubation period in hemophiliacs that is compatible to homosexuals and infected transfusion recipients ranges from 27 to 60 months[7].

Transfusion recipients: All types of component that is used for transfusion cause the efficient transmission of HIV from an infected donor to recipients. So the whole blood, packed cell platelets or frozen plasma all are equally like to serve as modes of transmission and it does appear to dependent on the type of component that is transfused[7].

In the United States, about 12,000 persons have acquired transfusion-associated HIV-infection between 1978 and 1984. Before 1984, HIV-infected donors present with seroprevalence of 0.04%. In New York City persons who were multiplied transfuse in the areas of high incidence were at increase risk of infection, although this overall low risks. The average HIV seroprevalence resulting from transfusion was 8%[7].

The seroprevalence of HIV-infection ranges from 8-10% increase in areas of Central Africa and this area have the risk of HIV transmission from blood is high. The implication of blood transfusion has been documented in Africa in AIDS patient, children born to seronegative mothers, hospital workers multiply transfused persons with sickle cell anemia[7].

Transfusion-related HIV transmission has been virtually eliminated in the United States by donor self deferral and implementation of screening serologies. HIV transmissions from donor that are infected but not seropositive have been documented in small amount. The situations in the developing country will not change until the effective screening test are widely available and medical misuse is abated[7].

Health care professionals: The risk of HIV infection in the heath care professional occurs sometimes. From the needlestick, exposure to blood from HIV-infected patient transmission is possible. Though this mode of transmission is possible, the risk is small. The seroconversion with AIDS of mucous membrane exposures to infected blood or body fluids[7].

Sexual transmission: The transmission of HIV by the sexual means appears to be considerably less efficient and highly variable[8,9]. A better understanding of the factors affecting transmission of HIV is required to develop effective prevention strategies. HIV infections create variability in transmission by sexual means and include biological differences in infectiousness, susceptibility or both, or differences in sexual behaviors. When analyzed in partner studies, the transmission rates approximately two or three times greater from infected males to females than from infected females to males[10].

Homosexual/ bisexual transmission: The leading risk category for HIV infection and AIDS for males in the United States and Europe is with the history of homosexual or bisexual behavior. Men without the history of IVDU who are homosexual or bisexual behavior represented 66% of all AIDS cases or 70% of all male AIDS cases in the United States. Homosexual or bisexual men who use IV drugs included another 8% of all reported cases[7] (Table 1).

The anal intercourse is a strong risk factor for HIV infection. From studies, it is revealed that receptive rather insertive anal intercourse possesses the greatest risk of HIV transmission[7,10]. It occurs by the way that the virus carried in the lymphocytes present in the semen and enters the recipient body through abrasions in rectal mucosa. Men rectally receptive with most or all their partners were at a four to seven fold risk for infection compared with those who were receptive with none or one partner, independent the number of partners. On the contrary, other risk behaviors such as douching before sex, use of dildos, or other activities that can cause trauma to the rectal mucosa were at two-to-three additional risk. Other causes of infection include with risks independent of number of partners and sexual practices associated prior infection with intestinal parasites and sexually transmitted disease (STD). There is a strong relationship exists between the STDs and transmission of AIDS[7]. The prevalence and incidence of HIV is considerably greater in-patients who present to STD clinics with genital ulcers and mucosal inflammatory disease and in a patient with a history of STD[10]. The risk was associated with giardiasis and syphilis. However, STDs facilitate HIV transmission by increasing genital shedding (infectivity) of HIV. There is a strong association in AIDS risk with number of sexual partners. When cases were compared with antibody negative, neighborhood controls were double with every 20-30 partners. The risk of HIV infection was doubled with every 30-40 partners when antibody negative neighborhood controls were compared. The drug such as nitrites increases tolerance to rectal abrasions or may facilitate infection through their vasodilator effect[7] .

The transmission of HIV by oral-genital, oral-anal is rare. The epidemiological studies of homosexual/ bisexual men the importance of practicing the "safe sex" for homosexual men and give advice in restriction of the number of sexual partners and avoidance of unprotected rectal sex[7].

Heterosexuals: For the transmission of HIV, the risk of vaginal intercourse appears to be considerably less than insertive anal intercourse. The heterosexual transmission is the principle mode of transmission in central Africa, Caribbean countries and in Asia. In United States, the ratio in AIDS cases for and women with a history of a primarily as a result of homosexual transmission is 13:1 as compared to ratio in Africa of near 1:1. The potentiality heterosexual transmission of HIV- infections is dependent upon the prevalence of the infection and the promiscuity of the population. Therefore, a critical risk factor for the spread of HIV in the heterosexual population is the heterosexual promiscuity[7]. In conclusion, it is apparent that heterosexual transmission exists in the United States; those areas where IVDU and heterosexual promiscuity are common.

Perinatal transmission: Women who have infection with HIV because of IVDU or heterosexual contact and are of child bearing age can be exposed to HIV infection. The mother-to-infant is the major cause of pediatric AIDS. Infected mothers can transmit the infection to their offspring by three routes:

- In uterus by transplacental spread
- During delivery through an infected birth canal and
- After birth by ingestion of breast milk[1].

Mucosal transmission: In the mucosal route of HIV transmission the exact source of HIV and the target cell in the mucosa of the recipient are still not known. The cellular fraction of semen contains spermatozoa, immature germ cells leukocytes (lymphocyte, granulocytes and macrophages) and epithelial cells. HIV can be detected in lymphocytes/ monocytes and cell free seminal plasma. Most of the cell-free HIV in seminal plasma arises distal to the vas deferens[10].

Table 1: U.S AIDS cases attributed to heterosexual transmission: May 30, 1988

Category		Number
Heterosexual cases, total 2574 (4% of total)	Male	1132
	Female	1142
Heterosexual cases since January 1988	Male	220
	Female	336
Multiple risk factors	Heterosexual and homosexual/ bisexual male	658
	Heterosexual and homosexual/ bisexual male, IVDU	240
	IVDU	1040
	Blood transfusion	128

Table 2: The normal level of some enzyme in blood

Name of the enzyme	Normal level (IU L^{-1})
Alkaline Phosphatase	30-90
Alanine Aminotransferase	5-40
Aspartate Aminotransferase	0-30
Lactate Dehydrogenase	0-200
Creatine Phosphokinase	0-200

Source: Pertel and Hirschtick[12]

Table 3: Some enzyme level in the patient AIDS and infected with *Mycobacterium avium*

Name of enzyme	Level measured (IU L^{-1})
Aspartate aminotransferase	54
Alanine aminotransferase	113
Alkaline aminotransferase	773

Table 4: Alkaline phosphatase and bilirubin level in AIDS patients infected with *Mycobacterium intercellulare*. Patient's age and sex have listed

Sex (F/M)	Age (Years)	Alkaline Phosphatase	Bilirubin
M	41	1666	0.3
M	35	2270	0.3
M	46	1740	3.4
F	27	1590	0.2

Source: Maldonado *et al.*[11]

HIV by the way similar to that as for neurological cells can infect the vaginal epithelial cells. The dendritic cell in the subepithelial tissue is sometimes direct target for HIV. HIV can be detected in endocervical swab specimens, cervicovaginal lavage samples and CD4 positive cell[10].

Other modes of transmission: The transmission of HIV infection cannot be occurred by environmental routes such as contaminated food or water, insect bites or causal personal and social contact in the household, workplace and in the school[1].

Biochemical manifestation in aids patients: After the infection with HIV, the people manifest many biochemical parameters, which are very important to measure the condition of the patient. The parameter that are important in this context are the enzymes such as the alkaline phosphatase, alanine aminotransferase, aspartate aminotransferase (AST), lactate dehydrogenase (LDH) and creatine phosphokinase (CK) are very important. The normal level of these enzymes are shown in Table 2.

With the development of AIDS the enzyme level listed above changes significantly. Among the above enzymes the alkaline phosphatase is a membrane bound enzyme located in the bile canalicular pole of the hepatocyte. In 1930, Roberts first described serum alkaline phosphatase elevation in-patients with hepatobiliary disorders[11]. The other enzymes with alkaline phosphatase are found in blood and can be measured easily. A patient with HIV seropositive for 4 years, the biochemical parameters were AST-84 IU L^{-1}, LDH-703 IU L^{-1}, CK-264 IU L^{-1}[12].

The patients with HIV are susceptible to infection with different microorganisms. Some of the common infections are pneumonia, *Mycobacterium avium* (MAC) complex, cytomegalovirus, Kaposi's sarcoma (KS) and pulmonary infection.

Infection with *mycobacterium avium*: Before the AIDS epidemics occurred, infection due to MAC was rare. However, 12,000 such infections among patients with AIDS have been reported in the past decade. A 39-year-old homosexual patient with MAC infection and several small KS lesions on his face and trunks have the following elevated enzyme level (Table 3)[13].

Infections also with the *Mycobacterium intercellulare* are also common in the patient with AIDS and have the following elevated alkaline phosphatase level (Table 4).

Infection with microsporidiosis: Microspridia are protozoan parasites that are responsible for significant gastrointestinal disease in-patients infected with HIV. A retrospective chart review between March, 1992 and March 1993 in Boston and Massachusetts showed elevated level of some biochemical parameter. Liver function test revealed that the mean level of aspartate aminotransferase and lactate dehydrogenase was 48 IU L^{-1} and 262 IU L^{-1} respectively. Alkaline phosphatase levels were greater then the upper limits of normal (106 IU L^{-1})[14].

Organ failure in aids patient: The person after infection with the HIV as become very susceptible may be infected with various microorganisms, which may be the cause of organ failure:

Respiratory failure in AIDS patient: The lung is the most common organ involved by opportunistic processes as the incidence of acute respiratory failure (ARF) in-patients with AIDS. In the early description of AIDS, nearly cases

Table 5: Comparison of clinical and laboratory characteristics of cases with acute respiratory failure and Cryptococcal disease vs. referents with Crypyococcal disease and no respiratory failure and infected with HIV

	No. (%) or Laboratory value per category	
Characteristic	Cases (n=19)	Referents (n=20)
Creatinine (mg dl^{-1})	2.1 (±2.4)	1.4 (±1.1)
LDH (IU L^{-1})	476.0 (±245.1)	264.0 (±128.6)
AST (IU L^{-1})	83.0 (±69.0)	52.6 (±34.5)
ALT(IU L^{-1})	42.9 (±36.5)	53.0 (±41.7)
Alkaline phosphatase (IU L^{-1})	274.7 (± 432.8)	103.3 (±70.3)

Source: Woods and Washington[15]

Table 6: Change in some enzyme level in-patient with HIV infection and respiratory failure

Characteristics	Level measured
Blood Urea Nitrogen	178.0 mg dL^{-1}
Creatinine	13.8 mg dL^{-1}
Bilirubin(Normal Value 1.3 mg dL^{-1})	5.1mg dL^{-1}
Alkaline Phosphatase	137.0 IU L^{-1}
Aspartate Aminotransferase	259.0 IU L^{-1}
Alanine Aminotransferase	85.0 IU L^{-1}
Creatine Kinase(Normal Value <170 IU L^{-1})	1.371 IU L^{-1}

Source: Onuchic *et al.*[16]

Table 7: Change in some enzyme level in-patient infected with HIV and liver abscesses

Characteristics	Measured level
Albumin	2.6 g dL^{-1}
Bilirubin	0.7 mg dL^{-1}
Alanine Aminotransferase	59.0 IU L^{-1}
Aspartate Aminotransferase	39.0 IU L^{-1}
Lactate Dehydrogenase	282.0 IU L^{-1}
Alkaline Phosphatase	140.0 IU L^{-1}
γ- glutamyl Transferase	37.0 IU L^{-1}

Source: Gunnarsson *et al.*[17]

of respiratory failure were due to *Pneumocystis carinii* pneumonia[15], but now a days other infections are frequent. In the hospital of Texas University, USA among 210 patient according to degree of infection with *Cryptococcosis*, manifesting biochemical parameters are presented in Table 5.

Respiratory associated with renal failure in AIDS patient: The AIDS patient with the disseminated infection may have the renal failure also. Such a patient of 31-year-old man with cocaine smoking manifested the following parameters[16].

Renal disease in chronically HIV- infected patient has been well described[18]. Acute HIV infection as a cause of renal failure is extremely rare. Acute retroviral infection that occurs about 40 to 70% of newly HIV infected people. It is self-limited with a usual duration of 2 to 30 days[16] (Table 6).

Liver abscesses in AIDS patient: The cause of liver abscess in-patient with AIDS is usually for the infection of *Staphyllococcus aureus* and *Mycobacterium tuberculosis*. Some of the biochemical parameter in-patients with liver abscess are shown in Table 7.

According to data from the Centers for Disease Control and prevention (CDC), 0.19-0.3% of patients with AIDS have had some form of nocardial infection[19]. Monica *et al.* observed a 27-year old male who was a parenteral drug abuser and found that his glucose level was 161mg dL^{-1}, protein level 9-g/dL and LDH level was 137 IU L^{-1}[20].

CD4+Cell Count in HIV Infected Person: The suppression of immune system is primarily affecting cell-mediated-immunity is the hallmark of AIDS. This affect causes a severe loss of CD4+T cells as well as impairment in the function of surviving helper T cells. Because depletion of CD4+T that is critical to the pathogenesis of AIDS[1].

There is abundant evidence that the CD4 molecule is infact a high affinity for receptor for HIV. This explains selective tropism of the virus for CD4+T cells and its ability to infect other CD4+T cells particularly macrophages. The binding gp 120 envelop glycoprotein to CD4 molecules is the initial step in infection, which is followed by fusion of the virus to the cell membrane and internalization. It is believed that fusion requires a post binding step in which viral gp 41 makes contact with a yet to be identified the cell membrane[1].

It might be surmised from the preceding discussion that productive infection of T cells is the mechanism by which HIV causes lysis of CD4+T cells. Despite the relentless and eventually profound, loss of CD4+ cells from the peripheral blood, however, there is relative paucity of productively infected T cells (0.01 to 0.1%) in circulation, especially early in the course of the disease[1].

HIV infects large number of CD4+ cells in lymphoid organs such as lymph nodes, tonsils and spleen[21,22]. Even in the early stages of HIV infection, approximately 20 to 30% of CD4+ cells in the lymph nodes are significantly greater than in peripheral blood.

In addition to cell death resulting from productive infection of CD4+T cells, several other indirect mechanisms could contribute to the loss of helper T lymphocytes. These include the following[1]:

- Loss of immature precursors of CD4+T cells either by direct infection of thymic progenitor cells or by infection of accessory cells that secret cytokines essential for CD4+T cell differentiation.
- Fusion of infected and uninfected cells, with formation of syncytia (giant cell). In tissue culture, the gp 120 expressed on productively infected cell binds to CD4 molecules on uninfected T cells, followed by cell fusion. Fused cells develop "ballooning" and usually die within a few hours.

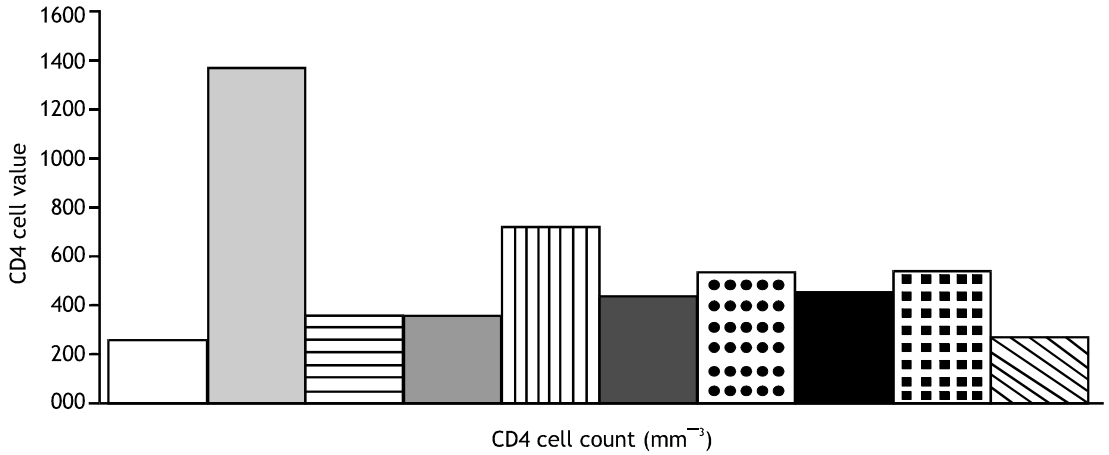

Fig. 1: CD4+ Cell counts in-patients infected with HIV. Each bar represents the different patient's CD4+ cell counts. The CD4+ cell counts remains high in HIV infected patients who do not show the symptom of AIDS[23]

- Autoimmune destruction of both infected and uninfected CD4+T cells. Soluble gp120 released from infected cells can bind to CD4 molecules on uninfected cells. Because many patients have circulating anti-gp 120 antibodies, these gp 120-coated cells could be destroyed by antibody dependent cellular cytotoxicity (ADCC).

The loss of CD4 cells by direct or indirect mechanisms leads to an inversion of the CD4/CD8 cell ratio in the peripheral blood. The normal ratio, which is close to two, may be changed in patients infected with HIV[1]. In a study a developed AIDS have the CD4 cell count was 95 mm^{-3} whereas the CD8 cell count was 107 mm^{-3} and the CD4/CD8 cell ratio was 0.9[16]. In conjunction with a positive HIV serology, a total CD4 cell count of <200 mm^{-3} or a CD4 percentage <14% fulfills the 1993 Centers for Disease control and Prevention (CDC) case definition of AIDS[23].

One of the important examples of HIV infection is the decrease in the CD4+ count at the time of acute infection, which on average decreases 30% to 40% from the baseline within two years of infection. Thus, selective reduction of the loss of CD4+ cells during acute HIV infection in vaccine recipient may provide an early indication of positive effect.

The CD4 lymphocyte count is currently the most important laboratory parameter in management and staging of patients infected with HIV. It is used for determining the risk of specific opportunistic infections[23] and for guiding the decision about antiretroviral therapy and prophylaxis for opportunistic infections. Despite the availability of other markers such as p24 antigen, β_2 microglobulin and most recently the quantitative values for viral load, depletion of CD4 cells appears to play a central role in pathogenesis of HIV related immunosuppression; hence, the use of CD4 count as an indicator of disease severity is biologically reasonable[17].

In conjunction with a positive HIV serology, a total CD4 cell count of <200 mm^{-3} or a CD4 percentage of <14% fulfills the 1993 Centers for Disease Control and prevention (CDC) case definition of AIDS[24]. This parameter is quantitatively meaningful: declining counts are associated with an increasing risk of opportunistic infections and death[25,26,27,28].

The loss of CD4 cell occurs due to the degree of development of AIDS in HIV infected persons. Usually during infection of HIV at very first CD4, cell count remains high but with the development of AIDS, it becomes low. For example in a study of hospitalized homosexual HIV seropositive patients, the CD4 cell counts declined from 582 to 315 mm^{-3}. In a second subject CD4, cell count dropped from 766 to 356/mm^3[29].

In a study in Michigan, nineteen patients were enrolled and divided into two groups namely group 1 and group 2 which was subsequently referred to as AIDS patients and HIV-infected patients. The CD4 cell counts were 45±60/mm^3 for the group with AIDS and 518±327/mm^3 for those with HIV infection. The following graph describes their CD4 cell count[23]:

Figure 1 indicates that the CD4 cell count remains high in the patients, but the in another study it reveals that with the development AIDS the cell count usually becomes low. It also indicates that after expressing AIDS the patient`s CD4 cell count may be high. It can be mentioned that according to CDC the normal count of CD4 cell is <200 mm^{-3}[23].

The CD4 cell count may vary with the test performed in the various laboratories. For example, a test was performed in four laboratories at Boston in the United

States with specimen collected from 24 patients revealed that the value varied significantly[23].

The range between laboratories (maximal value minus minimal value) per patient varied between 26 and 413 cells mm^{-3}. In addition, between laboratory variability in CD4 cell counts may occur due to secondary to numerous technical factors[23]:

- Temperature of the specimen,
- Interval from drawing of blood analysis,
- Anticoagulant used for collection,
- Specimen handling,
- Preparation of samples,
- Reagents and instruments used and
- Methods for standardization of the flow cytometer.

Table 8: CD4 cell counts in-patient infected with various organisms. Patient's age, sex and behavior have mentioned

Infection	Behavior	Age	Sex	Count	Reference
M. szulgai	Homosexual	42	Male	10 mm^{-3}	Rodriguez *et al.*, [20]
Nocardia asteroids	IVDU	27	Male	233 mm^{-3}	Holtz *et al.*, [19]
MAC	NF	30	Female	>500 mm^{-3}	Muelder and Nourou, [30]
Staphylococcus aureus	Homosexual	36	Male	20 mm^{-3}	Asmuth *et al.*, [14]
Yersinia enterolytica	NF	37	Male	206 mm^{-3}	Pertel and Hirschtick, [2]

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DISCUSSION

To develop effective transmission strategies, a better understanding of the factors affecting transmission of HIV is required[9]. In general, HIV transmission by any route is more likely when index case was found to have a greater degree of immunosuppression. As the mucosal route is an efficient mode of transmission attention should give on the strategy to increase mucosal antibody titer to prevent it. HIV is predominantly transmitted, as a cell-associated form is not known. In the macaque model, vaginal infection with SIV. HIV can be detected in lymphocyte/monocyte and cell free plasma. Interestingly, vasectomy does not result in a reduction of shedding of HIV in semen as measured HIV-RNA levels, indicating that most cell-HIV in seminal plasma arises distal to the vas deferens. However, in a study more than 1400 artificial insemination procedures with processed sperm from men with HIV failed to result in transmission of HIV indicates that the motile sperm fraction from semen is not likely to transmit the virus. Furuta *et al.* demonstrated that HIV could infect vaginal epithelial cells via CCD4 independent mechanism similar to the neurological cells. This mechanism involves initial interaction of the HIV-1 envelope with gp120 with cell-surface glycophosphingolipid which can be block by antibodies raised against gp120. Whether dendritic cell in subepithelial tissue can serve as direct target for HIV or are infected after a passage of the virus through the epithelial cell layer is not known. The relative contribution cell free and cell-associated HIV in sexual transmission remains under investigation[10].

There is sufficient evidence indicating a higher vertical HIV-1 transmission rate in the last trimester and during labour compared with the first trimester. Antiretroviral therapies either single or in combination given to the mother during the last trimester and delivery can reduce the viral load in maternal circulation. Appropriate timing and route of delivery can minimize vertical HIV-1 transmission during delivery. Elective caesarian section before the onset of labour with an intact bag of forewaters provides the least mother-to-fetus microtransfusion compared to other modes of delivery. In developing areas where malnutrition prevails, an adequate supply of essential micronutrients is proposed as an adjunctive measure to reduce HIV-1 perinatal transmission[31-33].

Depletion of CD4 cells appears to play a central role in the pathogenesis of related immunosuppression. Biological factors that have been associated with alteration in the CD4 cell count include age, season, time of day, ethnic origin, splenectomy status and drug use. For pediatric patient and for adults who have undergone splenectomy, higher baseline CD4 counts with correspondingly better immune function make threshold for prophylaxis established for adults with HIV infection inapplicable. For splenectomized adults it has been suggested that the CD4 percentage more precisely reflect immune function than the absolute CD4 count. For children infected perinatally, even adjusted CD4 count thresholds have proven ineffective in reducing the incidence of *Pneumocystis carinii* pneumonia (PCP); thus it has been recommended that all infants born to HIV infected mothers receive initial prophylaxis for PCP regardless of CD4 cell count. It shown in the present study interlaboratory variability remains a clinically significant problem, especially affecting individual clinical

decisions and diagnosis of AIDS[23]. Upon the infection of HIV when it become to propagate it destroys the lot of CD4 cell and opportunistic infection also causes the rise of various enzyme levels.

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