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Cd4+ CELL COUNTS IN THE PATIENTS OF HIV INFECTED IN SALEM

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ABSTRACT

Human ImmunoDeficienfy Virus(HIV) targets the CD4+ positive leading to cytopathic effects and chronic immune activation followed by eventual depletion of CD4+ lymphocytes and serve immune suppression. Treatment with combination antiretroviral therepy has lead to dramatic improvements in HIV-related morbidity and mortality.

The progressive depletion of CD4+ lymphoytes is the cardinal event in the pathogenesis during the infection by human immunodeficiency virus. The absolute number of these CD4+ T cells in the peripheral blood is the single most important parameter for monitoring tha disease associated with HIV infection.CD4+ Tcell enumeration is essential in three areas. First, CD4 counts are used to assess, The degree of immune deterioration as a surrogate marker for HIV induced damage and repeated CD4 tests define a decline slope of CD4 counts as an indication of the speed of progression towards Acquired Immuno Deficiency Syndrome (AIDS) , with the help of baseline CD4 counts , patients are placed for appropritate timing of starting antiretro viral therapy (ART) and to define the starting point for efficient prophylaxis against opportunistic infection . Secondly, while on therapy , improvement in CD4 counts is indicative of the efficacy of ART . Finally, epidermiological AIDS surveillance is based on CD4 counts to help define an anticipated welfare and health care needed .There is indeed an urgency to make it possible to deliver efficient therapy to patients at the right time, to guard against unmonitored drug distribution of resistance to commonly used drug and to dispel an out –dated myths that flow cytometry is too complex, Expensive and complicated for routine use in wide areas of the globe.

The successful ART is associated with potent suppression of HIV replication as measured by falling HIV/AIDS viral load and improvement in immune function with increased CD4+ lymphocyte numbers. Both previously sequestered memory CD4+ cells and naïve lymphocytes are involved in the immune reconstruction .

KEY WORDS: HIV ,ART , CD4+ cells

INTRODUCTION

The natural history of HIV infection is characterized by progressive decline in CD T – cell number and function that place infection persons at risk for opportunistic infection . In recent years significant immune reconstitution has been achieved by anti retro Viral(ART) resulting in a dramatic decline in HIV related morbidity and mortality (Christoph G . lemge *etal* .2003) .

The CD4 cell count is the best known, most studied and readily available prognostic marker. It is makes sense as a marker because decline in CD4 cell numbers is an effect of HIV, and CD4 T-cell depletion causes immune deficiency.

A normal CD4 cell count in the blood of a man without HIV infection will be in the range of approximately 400 to 1200 cells/mm^3 and 500 to 1600 cells/mm^3 in women. HIV is not the only

factor that can affect the CD4 cell count. Studies looking at CD4 cell counts in unifected, heterosexual and homosexual men and women found that –

(1) Women had higher CD4 cell counts that either heterosexual or homosexual men, by an average of 111 cells/mm^3.

(2) Women's CD4 cell counts fluctuate with the menstrual cycle.

(3) Oral contraceptive use was associated with a lower CD4 cell count.

(4) Smokers tended to have higher CD4 cell counts, by an average of 143 cells/mm^3.

(5) A good night's sleep decreases the number of CD4 T-cells and other immune system cells in the blood. However, the following afternoon and evening, a person who slept soundly has higher levels of CD4 cells than a person who experienced wakefulness during the night.

No racial differences were seen in one study (Maini 1996), but other studies have found differences.

A trend towards higher CD4 counts has also been seen in HIV-positive smokers, as compared with non-smokers. It may be deceptive for an untested person to use their CD4 cell count as a guide to whether or not they may be infected with HIV. A US study of HIV-negative patients admitted to an intensive care unit found that 17% had CD4 counts below 20, and the mean CD4 cell count was 510 cells/mm^3 (Aldrich A-cute illness other than HIV infection may also affect the CD4 cell counts, but it will not affect the CD4 : CD8 ratio, unlike HIV infection.

Only a small percentage of the total CD4 count is in the blood at any one time. The rest are in the tissues and lymph nodes. Changes described above may be due to the movement of CD4 cells between blood and tissues.

The CD4 cell count is a marker of likely disease progression, independent of viral load. Initially in HIV infection there is a sharp drop in the CD4 cell count and then usually stabilization around 500 to 600 cells/mm3. Both the extent of the early drop in the count and the level at stabilization are prognostic markers for the future risk of developing disease.

The best CD4 count to use to give an accurate prediction for the future is the most recent count Irregular counts (those unexpectedly high and low) may be laboratory errors or real temporary or sustained changes which should be checked by repeating the counts. It is estimated that for every fall of 100 cells/mm^3 in the CD4 cell count, the relative risk of developing AIDS is increased twofold. The absolute risk of developing AIDS, or not surviving, after having a particular count is changing over time as a result of treatment advances and other factors. A study of people with very low CD4 cell counts at Londons Royal Free Hospital found that in 1989 no patient survived with a count of zero, but by 1997 the average (medium) survival for people with zero counts was 1.2 years due to improved clinical care (Sabin 1997).

The CD4 cell count appears to decline more rapidly in the year before an AIDS diagonosis, and this is why treatment guidelines recommend that people with CD4 cell counts between 350 and 200 cells/mm^3 should consider treatment if their CD4 cell count begins to fall more rapidly (Schellekens 1992).

CD4 CELL IN THE AGE OF ANTIRETROVIRAL THERAPY

While viral load and CD4 cell count are both predictors of disease progression in untreated populations, there is evidence that CD4 cell count response on treatment is a better predictor of clinical outcome than viral load among people receiving antiretroviral therapy. In addition, CD4 cell count prior to treatment is crucial to response to treatment. That is, if a patient starts treatment with a CD4 cell count below 200 cells/mm^3, they are more likely to experience deteriorating health than if they start treatment when the CD4 cell count is above 200 cells/mm^3.

CD4 CELL COUNT AND RESPONSE TO TREATMENT

The link between baseline CD4 cell count and response to treatment in terms of viral load and clinical status is now well established.

Numerous studies have found that risk of disease progression is reduced among people who start antiretroviral therapy when their CD4 cell count is above 200 cells/mm^3. However, current

evidence indicates there is no clinical (health) benefit to starting treatment with a CD4 cell count above 350 cells/mm^3. Individuals who start treatment with a CD4 cell count below 200 cells/mm^3 are more likely to experience disease progression than people who start treatment earlier. The predictive value of CD4 cell counts prior to therapy is used as the basis for guidelines concerning when to start theraphy.

OBJECTIVE

To study the long-term immunological recovery in HIV – infected individuals receiving potent antiretroviral therapy (ART).

DESIGN

Prospective, observational study.

METHODS

Plasma HIV RNA, CD4 T lymphocyte counts were determined at 3 – 6 monthly intervals in 100 HIV infected subjects receiving ART, who suppressed plasma HIV RNA to levels below 400 copies/ml during a median observation period of 30 months from Jan 2006 to June 2008.

The analysis was based on data from 100 patients, who were followed for a median observation period of 30 months. Study participants had a age of 20 to 55 and they are from in and around the Salem district of Tamilnadu, India.

Among the patients, the reverse transcriptase (NNRTI) inhibitor regimen mainly consisted of stavudine and lamivudine, 65 were received and 20 were received zidovudine and lamivudine, 15 members were receiving the stavudine.

Stavudine → 15 + 65 → 80
Lamivudine → 65 + 20 → 85
Zidovudine → 20

Stavudine & Lamivudine → 65

Zidovudine & Lamivudine → 20

Antibodies 1 and 2, CD4 counts before and after ART treatment as follows:

Sl.No.	Type of HIV	CD4 Before ART counts	CD4 counts After ART
1	1	250	400
2	1	210	315
3	1	190	240
4	1	198	270
5	1	172	300
6	1	170	290
7	1	189	315
8	1	210	375
9	1	315	565
10	1	411	520
11	1	310	475
12	1	270	290
13	1	215	325
14	1	310	375
15	1	405	455
16	1	191	215
17	1	217	270
18	1	315	375
19	1	271	325
20	1	250	314
21	1	311	371
22	1	340	420
23	1	265	232
24	1	240	298
25	2	135	300
26	1	240	301
27	1	194	275
28	1	211	267
29	1	245	315
30	1	237	345
31	1	230	306
32	1	185	263
33	2	143	196
34	1	311	429
35	1	275	312
36	1	186	270
37	1	214	272
38	1	225	309
39	1	305	390
40	1	242	311
41	1	273	355
42	1	306	412
43	2	151	211
44	1	206	245
45	1	344	370

46	1	256	300
47	1	214	275
48	1	405	575
49	1	375	650
50	1	256	302
51	1	273	345
52	1	292	355
53	1	282	319
54	1	333	375
55	1	390	495
56	1	320	374
57	1	240	295
58	1	211	276
59	1	275	299
60	2	109	185
61	1	189	252
62	1	199	270
63	1	275	325
64	1	186	244
65	1	306	372
66	1	376	470
67	1	272	349
68	1	269	322
69	1	229	390
70	1	240	303
71	1	312	379
72	1	409	512
73	1	276	340
74	2	145	211
75	1	375	420
76	1	411	475
77	1	395	625
78	1	365	425
79	1	319	375
80	1	406	700
81	1	275	350
82	1	406	511
83	1	310	370
84	1	315	345
85	1	245	270
86	1	276	345
87	1	319	372
88	1	176	250
89	1	207	286
90	2	111	196
91	1	200	269
92	1	325	396
93	1	272	348
94	1	319	372
95	1	296	365
96	1	245	299
97	1	356	411
98	1	369	445
99	1	249	306
100	1	310	375

As the world enters the third decade of the AIDS epidemic, the evidence of its impact is obvious. Wherever the epidemic has spread unchecked, it is robbing countries of the resources and capacities on which human security and development depend. (Y.M. Tatfung *et.al* 2007).

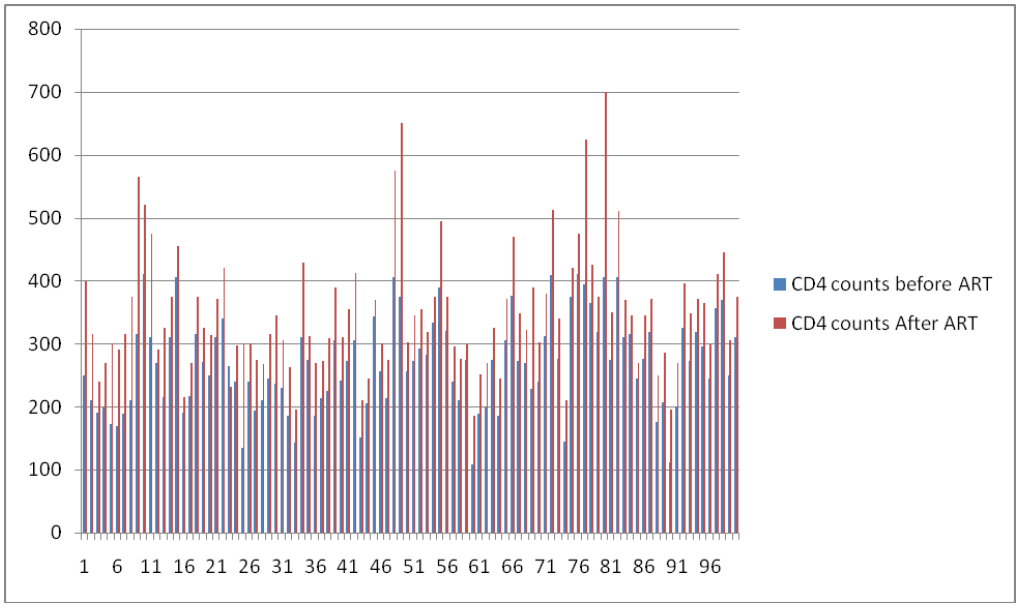
Potent antiretroviral therapy (ART) efficiently inhibits viral replication, resulting typically in a biphasic decline in plasma HIV RNA (HODD. Neumann Au. *et.al* 1995). The degree of viral load reduction in inversely associated with the short and medium-term increase in CD4 cell count. (Kaufmann D *et.al* 1998) allowing for a slow but gradual quantitative and qualitative recovery of the immune system (Autran *et.al* 1997 and Kelleher *et.al* 1996).

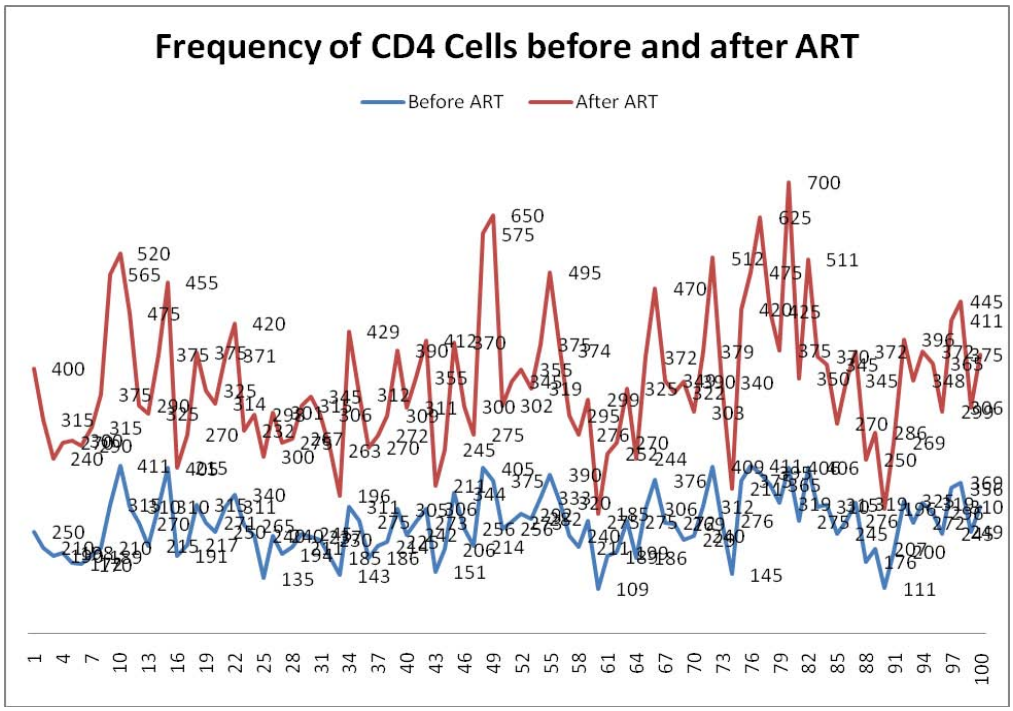
The CD4 T-lymphocyte response to ART is highly variable, which has resulted in early reports in discordant virological and immunological response. The reasons for the high variability of T-cell responses have been insufficiently studied and still remain unclear. It is conceivable that immunological as well as virological factors may be involved. In treatment, naïve individuals, a syncytium – inducing T-Cell tropic viral strain leads to a more rapid decline of CD4 T-lymphocytes than a macrophage, tropic strain. (Koot *et.al* 1993). As viral replication is not completely suppressed by ART (Lafeuillad *et.al* 1998 and Zhang L *et.al* 1990) a highly cytophathic viral strain may similarly impede the recovery of CD4 T-lymphocytes in individuals receiving ART (Renaud *et.al* 1999).

CD4 T-cell counts provide an indicator of immune competence in HIV disease, reasonably pre-ducting short-term risk for opportunistic infection.

The TLC are of limited value in predicting CD4 counts and should not be substituted for CD4 counts whenever possible (Mbanya *et.al* 2008).

Graphical Representation of CD4 counts -





CD4 T-cell recovery was satisfied by CD4 T-cell ART (>500 cells/μL was defined as a complete response as an incomplete response) determinants of incomplete were evaluated using logistic regression and survival. Individuals with incomplete CD4 T-cells more advanced HIV-1 infection at baseline. CD4 T-cell months of ART already reflect the capacity of the immune CD4 T-lymphocytes (Gibert *et.al* 2005).

Early detection of virological failure is important for optimal management of HIV – infected patients receiving ART. Patients who continue to receive a failing regimen are at risk of immunological failure, morbidity and death.

Moreover, accumulation of multiple antiretroviral drug resistance mutations may compromise the response to future drugs and fuel the spread of primary drug resistance within communities (Motasim Badri *et.al* 2008).

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