Original Research Article

Study of correlation between clinical profile, CD4 count and total lymphocyte count in HIV infected patients at rural tertiary care institute

Siddheshwar V. Birajdar[1], Sanjay S. Chavan[2], Deepak R. Patil[3*]

[1]Professor, [2]Associate Professor, [3]Resident
Department of Medicine, SRTR GMC, Ambajogai, India
[*]Corresponding author email: **drpatil3191@gmail.com**

International Archives of Integrated Medicine, Vol. 5, Issue 2, February, 2018.

Available online at http://iaimjournal.com/
ISSN: 2394-0026 (P) **ISSN: 2394-0034 (O)**
Received on: 01-02-2017 **Accepted on:** 11-02-2018
Source of support: Nil **Conflict of interest:** None declared.
How to cite this article: Siddheshwar V. Birajdar, Sanjay S. Chavan, Deepak R. Patil. Study of correlation between clinical profile, CD4 count and total lymphocyte count in HIV infected patients at rural tertiary care institute. IAIM, 2018; 5(2): 135-140.

Abstract

Background: India is a country with low HIV prevalence, yet it has the third largest number of people living with HIV/AIDS. Availability of antiretroviral medications is improving, making it is important to develop feasible strategies for the management of antiretroviral therapies in resource-limited settings.

Aim and objectives: To study clinical profile of HIV infected patients with special respect to total lymphocyte count (TLC) and CD4 count and study the correlation between Total Lymphocyte count (TLC) and CD4 count in HIV infected patients.

Materials and methods: An observational study was conducted on patients admitted in general medicine ward at the tertiary care hospital, fulfilling inclusion and exclusion criteria, for duration of 24 months. The detailed history and examination findings of the patients were recorded. To analyse the data we used statistical software SPSS 16.0 was used.

Results: Fever was the most common symptom reported. CD4 counts corresponded to various opportunistic infections. The Pearson correlation of TLC with CD4 counts was 0.388 i.e. moderate correlation at $p<0.05$ (0.005) and this showed the statistical high significance between TLC and CD4 count.

Conclusion: TLC is a widely available and inexpensive parameter, which can be used in place of CD4 count, for monitoring immune status in HIV infected individuals. TLC values may be useful, but less sophisticated and less costly methods of determining CD4 counts such as microvolume

fluorimetry and ELISA techniques be evaluated and made available for use in resource-limited settings.

Key words

Total Lymphocyte Count, CD4, HIV, Immunocompromised.

Introduction

Though India is a country with low HIV prevalence, it has the third largest number of people living with HIV/AIDS. As per HIV estimates in 2008-09, there are an estimated 23.9 lakh people living with HIV/AIDS in India with an adult prevalence of 0.31 percent in 2009 [1].

As the availability of antiretroviral medications improves, it is important to develop feasible strategies for the management of antiretroviral therapies in resource-limited settings [2]. In industrialized nations, changes in CD4 count and plasma viral load are used to determine the responses of the virus to antiretroviral therapy. Standard methods of CD4 count and plasma viral load enumeration require highly trained personnel and dollars of initial investment in laboratory instrumentation [3].

Citing the urgency of providing therapy on a wide scale and the financial and technological constraints to drastically upgrade laboratory facilities, the monitoring section of the guidelines stipulates that CD4 count testing is not available or too expensive for routine use, WHO recommends the use of Total Lymphocyte Count (TLC) to monitor the immune response to ART [4]. TLC is an inexpensive and widely available laboratory parameter. TLC is easily obtained from the routine complete blood count (CBC) with differential by multiplying percentage lymphocytes by leukocyte count.

In India, where the average annual income is < $ 350 (US), the cumulative cost of monitoring ART becomes a significant financial challenge [5]. In light of its low cost and widespread availability, TLC has already been a useful tool in low - income countries for predicting immunosuppression and triggering opportunistic infection prophylaxis [6-9].

However, there are fewer studies examining the change of TLC in patients on antiretroviral therapy [10]. While the total lymphocyte count correlates relatively poorly with the CD4 cell count in asymptomatic persons, in combination with clinical staging it is a useful marker of prognosis and survival [11-15]. WHO Global Programme on AIDS [20] proposed by WHO Staging system for HIV infection and disease strongly recommends TLC as an alternative indicator of HIV disease progression instead of CD4 cell count, where latter is not available, affordable and accessible [16].

The present study was carried out in rural tertiary care institute to assess the correlation between presenting symptoms and progression of the disease, which was monitored by a change in CD4 count and TLC.

Aim and objective

- To study clinical profile of HIV infected patients with special respect to Total Lymphocyte Count (TLC) and CD4 count.
- To study correlation between Total Lymphocyte Count (TLC) and CD4 count in HIV infected patients.

Materials and methods

This observational study was conducted on patients admitted in general medicine ward at the tertiary care hospital. The data for study was collected from subjects fulfilling inclusion and exclusion criteria. HIV positive patients admitted in the medicine ward over a period of 24 months were included in the study. Those patients on cytotoxic drugs, with connective tissue disorders,

not willing to participate in the study or Left Against Medical Advice (LAMA), were excluded from the study. The information collected was the detailed history and examination findings of the patients, investigation-findings like complete blood count, total lymphocyte count, CD4 count, LFT, KFT, BSL, X-ray chest, ultrasonography, CT scan.

Statistical analysis

To find the significance of the study parameters with variations with CD4 count, we used Pearson's correlation coefficient with other study parameters. $p<0.05$ was considered as statistically significant. To analyze the data we used statistical software SPSS 16.0 version to perform statistical analyses.

Results

From our study, it was found that, fever was the most common presenting symptom found in 36 (72%) of patients, followed by weight loss, with 35 (70%) of patients. Anorexia, cough, lethargy, diarrhoea, mouth ulcers, breathlessness and lymphadenopathy were the other common symptoms in our study population (**Table - 1**).

Table - 1: Presentation of Symptoms.

Presentation	No. of cases	%
Fever	36	72
Weight loss	35	70
Anorexia	31	62
Cough	14	28
Lethargy	12	24
Diarrhoea	8	16
Mouth ulcers	8	16
Breathlessness	5	10
Lymphadenopathy	5	10
Malaise	3	6
Skin infection	2	4

As shown in **Table - 2**, it was found that The CD4 counts were less than 100 /µl in 14 (28%) patients and between 101- 200/µl in 20 (40%), between 201-350/µl in 9 (18%) patients and more than 350/µl in 7 (14%) patients.

Table - 2: Distribution According to CD4 Count.

CD4 counts	Number	Percentage
<100	14	28
101 – 200	20	40
201 – 350	9	18
>350	7	14
Total	50	100

The lowest CD4 count recorded was 17 cells/µl and patient had oesophageal candidiasis. The highest CD4 count recorded was 626 cells/µl and the patients had tuberculous pleural effusion.

Our study pointed out that the study parameter total lymphocyte count shows upward trend with CD4 counts with p-value 0.019, total count shows mixed trend with CD4 counts, with the p-values being 0.22. This is depicted in **Table - 3**.

From **Table – 4**, it was found that the Pearson correlation of TC with CD4 count is 0.14 i.e. small correlation at $p>0.05$ (0.332) and which shows the statistical insignificance between TC and CD4 count. The Pearson correlation of TLC with CD4 counts is 0.388 i.e. moderate correlation at $p<0.05$ (0.005) and which shows the statistical high significance between TLC and CD4 count.

As seen from **Table - 5**, it was found that Total lymphocyte count cut off of ≤1500 cells /µl with CD4 count of ≤ 350 showed best sensitivity and specificity, compared to remaining TLC cut off as shown in the table with CD4 count <350 cells/cumm.

Discussion

The present study was done to assess the capability and clinical utility of the TLC change to serve as a surrogate marker for CD4 count change in monitoring patients, which has important implications for resource-limited settings. We correlated CD4 Count to Total Lymphocyte Count (TLC), which is available in all resource limited settings, to monitor disease progression in HIV infected persons.

Table - 3: Mean Pattern of Study Parameters with CD4 Counts.

Study Parameters Mean ± SD	**CD4 Counts**					**P value**
	<100	101 – 200	201 – 350	>350	Overall	
Total Count	7930.71	6668.50	6011.11	9942.86	7632	0.228>0.05 (NS)
	±4833.136	±2624.089	±2150.840	±3893.95	±3613.138	
Total Lymphocyte Count	1198.43	1257.60	1364.33	2174.43	1388.60	0.019 <0.05 (S)
	±812.672	±687.361	±761.851	±1036.477	±830.897	

Table - 4: Pearson Correlation of Study Parameters.

Study parameter	**Pearsons correlation (r)**	**P value**
Total counts	0.140	0.332 > NS
Total Lymphocyte Count	0.388	0.005<0.05 (HS)

Table - 5: TLC for CD4 Counts <350 Cells.

TLC	**Sensitivity (%)**	**Specificity (%)**	**PPV (%)**	**NPV (%)**
≤1000	20.59	93.75	87.5	35.71
≤1100	44.12	75	78.95	38.71
≤1200	50	68.75	77.27	39.29
≤1300	58.82	68.85	80	44
≤1400	67.65	62.5	79.31	47.62
≤1500	73.53	62.5	80.65	52.63
≤1600	76.47	43.75	74.29	46.67
≤1700	82.35	37.5	73.68	50
≤1800	82.35	37.5	73.68	50
≤1900	85.29	37.5	74.36	34.55
≤2000	88.24	37.5	75	60

Kumaraswamy, et al. [12] in their study, reported TLC as a useful tool for timing of opportunistic infection prophylaxis, in India and other resource constrained countries and concluded that TLC is a good enough surrogate marker for disease progression in HIV and can be used as a useful tool for the timing of opportunistic infection prophylaxis in HIV infected persons. In our study, fever was the most common presenting symptom with 36 (72%) of patients, followed by weight loss, which was the second commonest presenting symptom with 35 (70%) of patients. Fever (71%) and weight loss (65%) were reported to be the common presenting symptoms in a study conducted by S.K. Sharma too [17]. According to Sircar, et al. [18] fever, weight loss, diarrhoea and cough were the predominant clinical manifestations, which were consistent with our findings.

In our study, the total lymphocyte count showed positive trend to CD4 counts. The Pearson‘s correlation of total lymphocyte count and CD4 count was 0.388 i.e. moderate correlation at $p<0.05$ (0.005), which showed highly significant statistical correlation between TLC and CD4 counts. In a study conducted by Sreenivasan Srirangaraj, et al. [19] the correlation coefficient between TLC and CD4 count was r=0.34, which was similar to our study. However, in other studies, correlation coefficient between TLC and CD4 count reported in North America (r=0.77) 20, England (r=0.76)11 and India (r=0.744)7 were higher when compared with the results of

our study. This difference could be due to small sample size of our study.

We found that a TLC <1200 cells/µl had a 89.95% Positive Predictive Value (PPV), 41.37% Negative Predictive Value (NPV), 50% sensitivity and 75% specificity, for a CD4 count <200 cells/µl. This showed that the WHO [21] prescribed limit of TLC <1200 cells/µl as a surrogate for CD4 <200 cells/µl, according to our study, lacked sensitivity. Kumaraswamy, et al. [12] observed that with a TLC <1400 cells/µl, 73% of patients with CD4 cell counts <200 cell/µl (sensitivity 73%, specificity 88%, PPV 76%, NPV 86%) were identified. A study conducted by Gange, et al. [13] showed a significant correlation between TLC of < 1200 cells/µl to CD4 count < 200 cells/µl.

We further evaluated for a correlation between TLC and CD4 count <350 cells/µl. With a TLC cut-off of 1200 cells/µl, sensitivity was mere 50%, specificity 68.75%. With TLC <1200 cells/µl taken as the cut off, there existed a high chance of patients being misdiagnosed and not receiving therapy. An increased cut off for TLC improved the sensitivity with marginally lowering of specificity. With a TLC cut-off of 150 cells/µl, the sensitivity improved to 73.53%, with a specificity of 62.5%, PPV of 80.65% and NPV of 52.63%. The TLC cut off of 1500 also yielded the best sensitivity and specificity, compared to remaining TLC cut off with CD4 count <350 cells/µl. Our study correlated to Karanth, et al. [22] study, which recommended TLC <1500 cells/µl to CD4 count <350 cells/µl. Similar higher TLC cut off values were used in a study done by Jacobson, et al. [14], where he used a TLC <1900 cells/µl as cut off to predict CD4 count <350.

Limitations of our study include the modest sample size and fact that we only obtained single measurements of TLC and CD4. Our findings suggest that rather than shelve the use of TLC due to concerns of diagnostic utility, further research is needed to define optimum cut off values and should preferably be longitudinal with a much larger sample size.

Conclusion

We have demonstrated that TLC, is a widely available and inexpensive parameter, can be used in place of CD4 count, for monitoring immune status in HIV infected individuals. From present study it is clear that incidence of all disease expressions was increased with lower CD4 counts. In conclusion we recommend that the Management of HIV/AIDS in the HAART era should include focusing on using our resources as effectively and efficiently as possible to maximize the benefit. We recommend that while TLC values may be useful, that less sophisticated and less costly methods of determining CD4 counts such as microvolume fluorimetry and ELISA techniques be evaluated and made available for use in resource-limited settings.

References

1. Ministry of Health and family welfare, Department of AIDS control, Annual reports 2010-11. www.naco.gov.in/upload/REPORTS/NACO%20Annual%Report%2010-11.
2. K. Park, AIDS, Park‘s text book of preventive and social medicine. 22nd edition, Jabalpur: M/S Banarasidas Bhanot Publishers, 2005, p. 316 - 327.
3. Ministry Of health and Family Welfare. National AIDS Control Organization. Combating HIV/AIDS in India 2001.
4. Stephenson J. Cheaper HIV drugs for poor nations bring a new challenge: monitoring treatment. JAMA, 2002; 288: 151 -153.
5. Joint United Nations Programme on HIV/AIDS (UNAIDS)/ World Health Organization (WHO). AIDS epidemic update; December 2000. Geneva: UNAIDS/WHO, 2000. Publication UNAIDS/00. 44E-WHO/CDS/CSR/EDC/2000.9.
6. Mahajan AP, Hogan JW, Snyder B, Kumarswamy N, Mehta K, Solomon S,

Carpenter CC, Mayer KH, Flanigan PP. Changes in TLC as a surrogate for changes in CD 4 count following initiation of HAART; Implications for monitoring in resource limited settings. AIDS, 2004; 36(1): 567-575.

7. Kumaraswamy N, Flanigan TP, Mahajan AP, et al. Monitoring HIV treatment in the developing world. Lancet Infect Dis., 2002; 2: 656-657.
8. Montaner JSG, Le TN, Le N, et al. Application of the World Health Organization System for HIV infection in a cohort of Homosexual men in developing a prognostically meaningful staging system. AIDS, 1992; 6: 719-724.
9. Post FA, Wood R, Maartens G. CD 4 and Total Lymphocyte Counts as predictors of HIV Disease Progtression. QJMED, 1996; 89: 505-508.
10. Blatt SP, Luce CR, Butzin CA, et al. Total Lymphocyte Count as a Predictor of Absolute CD4 count and CD percentage in HIV infected persons. JAMA, 1993; 269: 622-626.
11. Beck EJ, Kupek EJ, Gompels MM, et al. Correlation between Total and CD 4 Lymphocyte Counts in HIV infection: not making the good enemy of the not so perfect. Int J STD AIDS, 1996; 7: 422-428.
12. Kumaraswamy N, MAhajan AP, Flanigan TP, et al. The Total Lymphocyte Count is a Useful tool for the Timing of Opportunistic infection Prophylaxis in India and other resource constrained countries. JAIDS, 2002; 31: 378-383.
13. Gange SJ, Lau B, Phair J, et al. Rapid declines in total lymphocyte count and hemoglobin in HIV infection begin at CD 4 lymphocyte counts that justify antiretroviral therapy. AIDS, 2003; 17: 119-121.
14. Jacobson MA, Liu L, Khayam-Bashi H, et al. Absolute or total lymphocyte count as marker for the CD 4 T lymphocyte criterion for initiating antiretroviral therapy. AIDS, 2003; 17: 917-919.
15. Spacek LA, Griswold M, Quinn TC, et al. Total Lymphocyte Count and hemoglobin combined in an algorithm to initiate the use of highly active antiretroviral therapy in resource-limited settings. AIDS, 2003; 17: 1311-1317.
16. Lau B, Gange SJ, Phair JP, et al. Rapid declines in Total Lymphocytes and hemoglobin concentration prior to AIDS among HIV-1 infected men. AIDS, 2003; 17: 2035-2044.
17. SK Sharma, Tamilarasu Kadhiravan, Amit Banga, Tarun Goyal, Indirsh Bhatia, Saha. Spectrum of clinical disease in a series of 135 hospitalized HIV – infected patients form North India. BMC Infectious, 2004; 4: 52.
18. Sircar AR, Tripathi AK, Choudhary SK, Misra R. Clinical profile of AIDS: a study at a referral hospital. J Assoc Physicians India, 1998; 46(9): 775-8.
19. Sreenivasan Srirangaraj, Dasegowda Venkatesha. Total lymphocyte count as a tool for timing opportunistic infection prophylaxis in resource – limited settings: a study from India. J Infect Dev Ctries., 2010; 4(10): 645-649.
20. Fournier AM, Sosenko JM. The relationship of total lymphocyte count to CD4 lymphocyte counts in patients infected with human immunodeficiency virus. Am J Med Sci., 1992; 304: 79-82.
21. World Health Organization. Antiretroviral therapy for HIV infection in adults and adolescents: Recommendations for a Public Health approach. 2010. www.who.co.in.
22. Suman S. Karannth, MR Rau, Anurag Gupta, Asha Kamath, Vikram Shanbhogue, BC Pruthvi. Utility of total lymphocyte count as surrogate for absolute CD4 count in the adult Indian HIV population; A prospective study. Avicenna J Med., 2014; 4(1): 1-4.