ORIGINAL RESEARCH PAPER
Volume - 11 | Issue - 02 | February - 2022 | PRINT ISSN No. 2277 - 8179 | DOI : 10.36106/ijsr
INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

STUDY CORRELATION BETWEEN, TOTAL LYMPHOCYTE COUNT, CD4 COUNT & CLINICAL PROFILE OF HIV INFECTED PATIENTS AT TERTIARY CARE INSTITUTE

Internal Medicine

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ABSTRACT

INTRODUCTION As per HIV estimates in 2018-19, there are an estimated 33.9 lac people living with HIV/AIDS in India with an adult prevalence of 0.51 percent in 2019. Citing the urgency of providing therapy on a wide scale and the financial and technological constraints to drastically upgrading laboratory facilities, the monitoring section of these guidelines stipulates that CD4 count testing is not available or too expensive for routine use, WHO recommends the use of Total Leukocyte Count (TLC) to monitor the immune response to ART. 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. The present study is done is being done in tertiary care institute to assess the correlation between presenting symptoms and progression of the disease, which is monitored by a change in CD4 count and TLC. **AIMS & OBJECTIVES** To study clinical profile of HIV infected patients with respect to Total Lymphocyte count and CD4 count & to study correlation between Total Lymphocyte count and CD4 count in HIV infected patients.**MATERIAL & METHODS** Observational study conducted on patients admitted in general medicine ward at tertiary care hospital over a period of 24 months duration. **OBSERVATIONS & RESULTS** From our study, it was found that, fever was the most common presenting symptom in our study with 36 (72%) of patients, followed by weight loss, which was the second most common presenting symptom in our study with 35 (70%) of patients. Anorexia, cough, lethargy, diarrhoea, mouth ulcers, breathlessness and lymphadenopathy were the other common symptoms in our study population. 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. **DISCUSSION** The present study is 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. 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.

KEYWORDS

INTRODUCTION

Though India is a country with low HIV prevalence; it has the third largest number of people living with HIV/AIDS. Recent results from an Avahan study of sex workers in Karnataka showed that from the time the HIV prevention programme was first implicated; the HIV prevalence in this population group declined from 20% to 16% and condom usage increased from 66 to 84%.(1) 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. (2)

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 southern India, for example, the cost of a single TLC from a CBC is < $1 (US).

In India, where the average annual income is < $ 350 (US), the cumulative cost of monitoring ART becomes a significant financial challenge.(3) In light of its low cost and widespread availability, TLC has already been a useful tool in low - income countries for predicting immune-suppression and triggering opportunistic infection prophylaxis.(4-7) Angelo et al(8) in their study, ―Evaluation of TLC as a substitute for CD4 count in the follow up of AIDS patients have shown that TLC has a high specificity to indicate patients for prophylaxis. Mahajan et al.(9) in their study, changes in Total Lymphocyte Count as a Surrogate for Changes in CD4 count following initiation of HAART. The present study is done is being done in tertiary care institute to assess the correlation between presenting symptoms and progression of the disease, which is monitored by a change in CD4 count and TLC.

AIMS & OBJECTIVES

1. To study clinical profile of HIV infected patients with respect to Total Lymphocyte count and CD4 count.
2. To study correlation between Total Lymphocyte count and CD4 count in HIV infected patients.

MATERIAL & METHODS

Source of data: Study conducted on patients admitted in general medicine ward at tertiary care hospital

Sample Size:
HIV positive patients admitted in medicine ward over a period of 24 months duration.

Sampling Method:
Universal sampling method.

Study Design:
Observational study.

Inclusion Criteria:
All HIV positive patients in the medicine ward of the tertiary care institute during the period of study.

Exclusion Criteria:
- Cases on cytotoxic drugs and Cases with connective tissue disorders.
- Cases not willing to participate in the study
- Cases Left Against Medical Advice (LAMA)

Statistical analysis:
To analyse the data we have used statistical software SPSS 16.0 version to perform statistical analyses.

Ethics permissions:
The work on this study began after obtaining the approval of the Institutional Ethics Committee (IEC).

OBSERVATIONS & RESULTS

It was found that, fever was the most common presenting symptom in our study with 36 (72%) of patients, followed by weight loss, which was the second most common presenting symptom in our study with 35 (70%) of patients. Anorexia, cough, lethargy, diarrhea, mouth ulcers, breathlessness and lymphadenopathy were the other common symptoms in our study population.

The CD4 counts were less than 100 /µl in 14 (28%) patients and between 101- 200/µl in 20 (40%), between201-350/µl in 9 (18%) patients and more than 350/µl in 7 (14%) patients.The lowest Cd4 count recorded was 17 cells/µl and patient had esophageal 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.

Table: 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)

From table - 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.

Table: 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

A s seen from above table - 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 is 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.

In view of the high costs and limited availability of resources to estimate absolute CD4 counts, the need for simpler and relatively accurate markers of disease progression through laboratory investigations are felt.

We are correlating CD4 Count to Total Lymphocyte Count, which is available in all resource limited settings, to monitor disease progression in HIV infected persons. Throughout the course of chronic HIV infection, the number of CD4 lymphocytes is depleted, and the loss of these cells is associated with development of characteristic opportunistic infections and malignancies of AIDS. (10, 11) Clinical staging can be based on either the CD4 percent or the CD4 count. However, most clinical studies have used the absolute CD4 count, even though the percentage value is less subject to fluctuations. (12,13) Kumaraswamy et al.(14) in their study, TLC as a useful tool for timing of opportunistic infection prophylaxis in India and other resource constrained countries 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, the total lymphocyte count showed positive trend to CD4 counts. The Pearson's correlation of total lymphocyte count and CD4 count is 0.388 i.e. moderate correlation at p<0.05 (0.005), which shows highly significant statistical correlation between TLC and CD4 counts.

In a study conducted by Sreenivasan Srirangaraj et al(15) the correlation coefficient between TLC and CD4 count was r=0.34, which is similar to our study.However, in other studies, correlation coefficient between TLC and CD4 count reported in North America (r=0.77),(16) England (r=0.76)11 and India (r=0.744) were higher when compared with the results of this 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% PPV, 41.37% NPV, 50% sensitivity and 75% specificity, for a CD4 count <200 cells/µl. This shows that the WHO (17) prescribed limit of TLC <1200 cells/µl as a surrogate for CD4 <200 cells/µl, according to our study, lacks sensitivity. Kumaraswamy et al. (3) 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.

Our study correlated to Suman S. Karanth et al (18) study which recommended TLC <1500 cells/µl to CD4 count <350 cells/µl. Similar higher TLC cut off values have been used in a study done by Jacobson et al.(19), where he used a TLC <1900 cells/µl as cut off to predict CD4 count <350 The CD4 counts were less than 200 cells/µl in 34 (68%) of the patients in our study.

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. HIV clinics should come up in the peripherals and the physicians treating the HIV patients should be involved in the management of such patients making use of the cheaper and alternate biological markers. Further studies should be encouraged to evaluate HIV-infected patients for various biological markers choose from them a set of markers that can effectively evaluate the disease state and probable time due for progression to AIDS and formulate effective intervention strategies in the management of HIV disease.

Tuberculosis followed by oral candidiasis and diarrhea were the major Opportunistic Infections (OIs) encountered by HIV-infected patients. CD4 count less than 200/mm3 and WHO clinical stage III and IV were found to be strongly associated with prevalence of OIs. Interventions aimed at preventing and treating HIV associated OIs is crucial. Commencement of ART should be encouraged before the patients' CD4 count drops below 350/mm3 since the local practice is different from the WHO's recommendation for the commencement of ART in few areas.

There was a highly significant correlation between CD4 count and total lymphocyte count. CD4 counts are the gold standard in assessment of disease progression in HIV infected persons. Total lymphocyte count can be used as a surrogate marker in resource poor countries. Thus, for the people who may not be able to afford the investigations and treatment, total lymphocyte count can serve as a cost effective, affordable index to start ART and also to monitor ART in HIV infected persons.

Hence 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 availabl for use in resource-limited settings. 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. Considering the significantly higher cost of performing a CD4 count relative to TLC, and the limited availability of facilities, efforts that will lead to adoption of TLC will remove a major barrier to HAART initiation for HIV infected patients in resource poor setup.

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