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USEFULLNESS OF TOTAL LYMPHOCYTE COUNT (TLC) AS A ANALYTICAL MARKER FOR CD4 T CELL COUNT IN HIV INFECTED PATIENTS: A HOSPITAL BASED STUDY

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ABSTRACT

AIDS is not a single disease but it is the manifestation of a group of diseases, therefore it is appropriately called as syndrome. Due to infection the immune mechanism breaks down making the host vulnerable to overwhelming fatal infections. HIV primarily causes progressive qualitative and quantitative deficiency of a subset of T lymphocytes called CD4 T cells. CD4 T cell count has become the most quoted single index of cell mediated immunity in HIV infected patients. However, providences in resource-constraint settings may not have access to the well established laboratory measurement, or the cost may be prohibitive resulting in the need for an alternative and effective surrogate marker. Hence, total lymphocyte count (TLC) was evaluated as a probable surrogate marker for CD4 T cell count in this study. **Aims:** To evaluate the correlation of CD4 T cell count with the Total Lymphocyte Count in HIV infected patients and to find out a critical value of TLC which can predict a CD4 T cell count less than 200/cmm, for the initiation of antiretroviral therapy. **Materials and Methods:** The prospective study was conducted on the 40 HIV positive patients admitted in the Department Medicine over a period of one year at Indira Gandhi Medical College and Hospital (IGMC) Shimla. The Complete Blood count, CD4 T cell count and Total Lymphocyte count were measured. The Sensitivity, specificity and positive predictive value of Total Lymphocyte count computed to find out CD4 T cell count <200/cmm. using spearman' s rank correlation. **Results:** A positive correlation between Total Lymphocyte count and CD4 T count was observed in our study. The Total Lymphocyte count of 1700/cmm was able to predict CD4 T cell count <200/cmm with highest sensitivity (72%), specificity (100%) and positive predictive value (100%). **Conclusions:** The Total Lymphocyte count 1700 cells/ cmm was the best predictor of CD4 count <200 cells/ cmm and hence TLC can become a reliable marker for the initiation of Antiretroviral therapy resource limited country.

KEYWORDS: Total lymphocyte count, CD 4 T cell, antiretroviral therapy.

INTRODUCTION

Human immunodeficiency virus epidemic had been evolving in India since the first case was detected in Tamil Nadu in 1986. The diagnosis of HIV infection can be intriguing as the laboratory diagnosis may not be possible in the developing and underdeveloped countries due to lack of resources, therefore there is a need for affordable and reliable marker for the initiation and monitoring of treatment in AIDS patients. The CD 4 T cell count is done by flow cytometry which is expensive investigation may not be feasible in every centre treating HIV infection in the resource limited countries. The total lymphocyte count can be easily derived from a routine white cell count in resource poor countries and hence become a surrogate marker for treatment with ART.

There are approximately 36.7 million people currently living with HIV and tens of millions of people have died of AIDS-related causes since the beginning of the epidemic [1,2]. While new cases have been reported in all regions of the world, mostly from the under developed and developing nations. India has the third largest HIV epidemic in the world. In 2015, HIV prevalence in India was an estimated 0.26% [3] and an estimated 68,000 people have died from AIDS related illness [4]. Many people living with HIV or at risk for HIV do not have access to prevention, care and treatment, and there is still no cure. HIV primarily affects those in their most productive years; about a third of new infections are among young people (ages 15-24). [1,2]

In HIV many clinical and laboratory markers have been used to estimate prognosis in patients with HIV-1

infection. Identification of laboratory markers that help to predict, progression to AIDS in people infected with HIV are desirable because of the implications for both clinical management and counselling of the patient. The single best predictor of AIDS onset identified so far is the percentage or absolute number of circulating CD4+ T cells.

However, providences in resource-constraint settings may not have access to this laboratory measurement or its cost may be prohibitive resulting in the need for an alternative, surrogate marker. Estimation of plasma viral loads is another reliable measure of the immune status and disease stage of HIV-infected patients. In the absence of viral loads and CD4 counts for monitoring HIV disease, the value of total lymphocyte count (TLC) as a surrogate for CD4 T cell count has been argued.

Thus, a surrogate marker for CD4 T cell count, if proven reliable, can provide a tool for monitoring disease status in the underdeveloped nations where the bulk of the HIV patients are present. With better awareness about the immune status of the HIV-infected individuals through available reliable laboratory markers, an early diagnosis of Opportunistic infections (OIs) can be made and highly active antiretroviral therapy (HAART) can also be instituted at an early stage.

Thus, the present study was undertaken to evaluate the correlation of TLC as a surrogate marker for CD4 T cells in resource limited areas. The goal is to start the ART in the newly diagnosed HIV patients based on the total lymphocyte count obtained from HIV positive blood sample at the attached centre rather than travelling to have CD4 count results done at the distant places. The delay associated with such arrangement has been responsible for increased morbidity and mortality among HIV infected patients due to delay in initiation of highly active antiretroviral therapy, loss of follow up, non compliance leading to immunological failure.

MATERIALS AND METHODS

Study design and Subjects

The prospective study was conducted in the inpatient department of Medicine over a period of one year at Indira Gandhi Medical College Shimla.

The symptomatic HIV infected patients admitted in the medicine wards were included in the study. The diagnosis of HIV infection was made as per the National Guidelines for HIV screening and testing based on Elisa, Rapid and Simple (ERS) approach along with pre and post test counselling.

The complete blood count, liver function test, renal functions and CD4 T cell count estimation was carried out by Fluorescent Activated Cell Sorter System. The TLC was derived by multiplying the total leukocyte count by the percentage of lymphocytes.

The Spearman's Rank correlation was done between CD4 T cells and total lymphocyte counts.

RESULTS

The data was collected from 40 HIV infected admitted patients and analyzed. The age and sex distribution is shown in the (Table 1). The majority of the patients were in the age group of 31-40 years (47.5%), followed by less than 30 years (32.5%). The majority of patients were male 30(75%) and 10(25%) were females in the study.

Table 1: Age and sex distribution

S.No	Age (years)	Male	%age	Female	%age
1	<30	7	17.5	6	15
2	31-40	17	42.5	2	5
3	41-50	5	12.5	2	5
4	>50	1	2.5	0	0
5	Total	30	75	10	25

Total lymphocyte count was done in 38(95%) patients and CD 4 T count was done in 34(85%) patients. The distribution of total lymphocyte count (Table 2) and 70% of the patients were having TLC count less than 2000/cmm. The distribution of CD 4 T cell count (Table 3) and 85% of patients were having CD 4 T cell count less than 200/cmm.

Table 2: Distribution of Total Lymphocyte Count

Sr No	Total lymphocyte count	No of patients (n=38)
1	< 500	4
2	501-1000	7
3	1001-1500	12
4	1501-2000	4
5	2001-2500	6
6	>2500	5

Table 3: Distribution of CD4 T Cell Count

Sr No	Total CD4 T cell count	No of patients (n=34)
1	<50	10
2	50-100	10
3	101-150	8
4	151-200	1
5	201-250	1
6	251-300	1
7	300-350	1
8	351-400	0
9	401-450	2

Spearman,s rank correlation was analyzed between CD4 T cell count and total lymphocyte count(rs=.758) Correlation was significant at the .01 level. Correlation was higher in male patients as compared to female patients. (Table 4)

Senstivity, specificity and positive predictive value were compared for TLC ranging from 1000-2000 cells/cmm to detect CD4 T cell count <200/cmm. A TLC cut-off of <1700 cells/cmm had a PPV of 100 %, 72% sensitive and 100% specific for a CD4 T count <200 cells/cmm. Thus, it had the best predictive value and was most sensitive in predicting a CD4 count of <200 cells/cmm while not compromising on its specificity. (Table 5)

Table 4: The correlation between CD4 T cell count and Total Lymphocyte Count

Spearmans rank correlation	Lymphocytes	CD4 T cell count
Correlation coefficient	1.000 0.758	0.758 1.000
Significance Lymphocyte CD 4 cell	.000	.000
N Lymphocyte CD 4 cell	38 34	34 34

Table 5: The Distribution of sensitivity, specificity, positive predictive value of Total Lymphocyte and CD4 T cell count

S.No.	Lymphocytes	CD4 Cells	Senstivity	Specificity	PPV
1	1000	200	27	80	88.8
2	1100	200	51	100	100
3	1200	200	44	80	92
4	1300	200	58	100	**100**
5	1400	200	58	**40**	**85**
6	1500	200	68	**100**	**100**
7	1600	200	65	40	**86**
8	1700	200	72	100	**100**
9	1800	200	75	80	**95**
10	1900	200	79	**80**	**95**
11	2000	200	92	**75**	**86**
12	1700	350	64	**66**	**95**

DISCUSSION

Several studies have been done all over the world to find correlation between TLC and CD4 cell count. In our study correlation between Total lymphocyte count and CD 4 cell count was 0.758. This observation is comparable to the studies done by Kaushik et al[5], Shapiro NI et al[6], VanDer Ryst et al[7],PB Agrawal et al[8] and Karanth SS et al[9], (Table 6).

Table 6: Comparison of Total lymphocyte count and CD4 T cell count in Present study with others studies

STUDY	Number of patients	Correlation
Present study	40	.758
Kaushik et al	108	.5
Shapiro NI et al	807	.69
VanDer Ryst et al	2777	.70
PB Agrawal et al	61	.327
Karanth SS et al	200	.682

A good correlation between the two variables has also been observed by other studies conducted across the world viz Kumaraswamy et al., in India[10] (r = 0.744), England[11] (r = 0.76), North America[12] (r = 0.77), South Africa[7] (r = 0.70), Uganda[13] (r = 0.73), and London[14] (r = 0.70).

In our study Total lymphocyte count of 1200 cells/cmm was able to detect CD4 T cell count <200/cmm with sensitivity of 44%, specificity 80% and positive predictive value of 92%. This was comparable to the other studies Daka et al[15] , Angelo ALD et al[16] , PB Agrawal et al[6] as shown in table 7.

Table 7: Comparison of sensitivity and specificity of Total Lymphocyte Count and CD4 T Count

Study	Senstivity	Specificity
Present study	44%	80%
Daka et al	41%	83.3%
Angelo ALD et al	46.5%	92.8%
PB Agrawal et al	34.48%	67.50%

In our study using higher total lymphocyte count as cut off sensitivity increased from 27%-92% detecting patients with CD4 cell count <200/cmm. This is in accordance with studies done by Sharipo NI et al[6] (67%-96%) and Sonali J et al[17] (30.61%-97.27%).

In our study sensitivity, specificity and positive predictive value were maximum at TLC <1800/cmm. Using TLC 1800/cmm as cut off 75% of patients with CD 4 cell count <200/cmm will be detected, 25% would have been falsely detected to have CD4 cell count <22/cmm. So 95% of those with TLC <1800 will have CD 4 T cell count <200/cmm (PPV 95%). these observations are similar to other studies like Karanth S et al[7], Sreenivasan et al[18] , Agrawal PB et al[6], Angelo ALD et al[16] , Daka et al[15] shown in (Table 8).

Table 8: Comparison of TLC, Sensitivity and specificity

Studies	TLC Cut –off	Sensitivity	Specificity
Present study	<1800	75%	80%
Karanth S et al	<1500	82%	88.2%
Sreenivasan et al	<1520	71.08%	78.26%
PB Agrawal et al	<1643	93.93%	20%
Angelo ALD et al	<1700	59.4%	75.8%
Daka et al	<1780	61%	62%

Total lymphocyte count can be used as a marker of disease progression ,to start antiretroviral therapy and monitor it. We can also use TLC count to start prophylaxis for opportunistic infections. Variations in the cut off values of TLC in various studies as well as in our study may be due to difference in sample size, or may also be due to different ethnic, racial, epidemiological and socioeconomic factors.

CONCLUSION

The routine use of CD4 T cell count and plasma viral load in the management of HIV infection is not possible in remote areas in the resource limited countries. So use of total lymphocyte count in the management of symptomatic HIV positive patients may be undertaken and more studies with large sample size should be planned to establish the validity of total lymphocyte count as a proxy measure of CD4 T cell count. So findings of this study conclude there is a positive correlation between CD4 T cell count and Total lymphocyte count. Hence total lymphocyte count can be used as cost effective surrogate marker to start and monitor treatment of HIV infected patients.

REFERENCES

1. United Nations Programme on HIV and AIDS. Global AIDS Update. 2016, http://www.unaids.org
2. United Nations Programme on HIV and AIDS. Epidemiology Slides; 2016 http://www.unaids.org
3. National AIDS Control Organisation. Department of AIDS Control. Ministry of Health and Family Welfare. Annual Report.2015-16, http://www.naco.gov.in
4. United Nations Programme on HIV and AIDS. Prevention Gap Report 2016, http://www.unaids.org
5. Kaushik P, Kaushik R, Pande JN. Usefulness of total lymphocyte count as a surrogate estimation of the CD4 lymphocyte count in patients of suspected AIDS. J Assoc Physicians India 1997; 45: 455–6.
6. Shapiro NI, Karras DJ, Leech SH,Heilpern KL.Absolute lymphocyte count as a predictor of CD 4 count. Ann Emerg Med 1998; 32: 323-328.
7. Van der Ryst E, Kotze M, Joubert G, Steyn M, Pieters H, van der Westhuizen M, van Staden M, Venter C: Correlation among total lymphocyte count, absolute CD4+ count, and CD4+ percentage in a group of HIV-1-infected South African patients. J Acquir Immune Defic Syndr Hum Retrovirol. 1998; 19(3): 238-244.
8. Agrawal PB, Rane SR, Jadhav MV. Absolute Lymphocyte Count as a Surrogate Marker of CD4 Count in Monitoring HIV Infected Individuals: A Prospective Study. J Clin Diagn Res. 2016 May; 10(5): EC17-9.

9. Karanth SS , Rau NR, Gupta A, Kamath A, Shanbhogue V , Pruthvi BC. Utility of total lymphocyte count as a surrogate for absolute CD4 count in the adult Indian HIV population: A prospective study. Aviceenna J Med. 2014 Jan; 4(1):1-4.
10. Kumarasamy N, Mahajan AP, Flanigan TP, Hemlatha R, Mayer KH, Carpenter CC, et al. Total lymphocyte count (TLC) is a useful tool for the timing of opportunistic infection prophylaxis in India and other resource-constrained countries. J Acquir Immune Defic Syndr 2002; 31: 378-83.
11. 11. Beck EJ, Kupek EJ, Gompels MM, Pinching AJ. Correlation between total and CD4 lymphocyte counts in HIV infection: Not making the good an enemy of the not so perfect. Int J STD AIDS 1996; 7: 422-8. 7. Fournier AM, Sosenko JM. The relationship of total lymp Prasad KN, Nag VL, Dole TN, Ayyagari A. Identifi cation of enteric pathogens in HIV-positive patients with diarrhoea in northern India. J Health Popul Nutr 2000; 18: 23-6.
12. Fournier AM, Sosenko JM. The relationship of total lymphocyte count to CD4 lymphocyte counts in patients infected with human immunodefi ciency virus. Am J Med Sci 1992; 304: 79-82.
13. Kamya MR, Semitala FC, Quinn TC, Ronald A, Njama-Meya D, Mayanja-Kizza H, et al. Total lymphocyte count of 1200 is not a sensitive predictor of CD4 lymphocyte count among patients with HIV disease in Kampala, Uganda. Afr Health Sci 2004; 4: 94-101.
14. Prasad KN, Nag VL, Dole TN, Ayyagari A. Identifi cation of enteric pathogens in HIV-positive patients with diarrhoea in northern India. J Health Popul Nutr 2000; 18: 23-6.
15. Daka D, Loha E. Relationship between total lymphocyte count (TLC) and CD4 count among peoples living with HIV, Southern Ethiopia: a retrospective evaluation. AIDS Research and Therapy. 2008; 5: 26.
16. Angelo ALD, Angelo CD, Torres AJL, Ramos AMC, Lima M, Netto EM, et al. Evaluating total lymphocyte counts for CD4 counts in the follow up of AIDS patients. Braz J Infect Dis. 2007; 11(5): 466–70.
17. Jain S, Singh AK, Bajaj J, Singh RP, Damle AS. Evaluation of total lymphocyte count (TLC) as a surrogate marker for CD4 count in HIV-positive patients for resource-limited settings. Muller J Med Sci Res 2015; 6: 23-6.
18. Sreenivasan S, Dasegowda V. Comparing absolute lymphocyte count to total lymphocyte count, as a CD4 T cell surrogate, to initiate antiretroviral therapy. J Glob Infect Dis. 2011; 3(3): 265–68.