CORRELATION BETWEEN CLINICAL PROFILE, TOTAL LYMPHOCYTIC COUNT AND CD4 COUNT IN HIV POSITIVE PATIENTS

Atul Vijayrao Rajkondawar[1], Vinayak Rodge[2]

[1]Associate Professor, Department of General Medicine, Government Medical College, Nagpur.
[2]Senior Resident, Department of General Medicine, Government Medical College, Nagpur.

ABSTRACT

BACKGROUND

HIV infection can be monitored by laboratory and clinical markers of disease progression. In the absence of CD4 count, the use of total lymphocyte count has been advocated to predict CD4 count and to stage HIV disease. The present study was undertaken to determine whether the TLC accurately predicts the CD4 count in HIV positive patient and its clinical correlation.

MATERIALS AND METHODS

A total of 100 HIV positive patients of age less than 12 years and who were attended ART clinic/outpatients and inpatients at tertiary care hospital were included in the study and were subjected to clinical examination and relevant investigations including CD4 count and TLC.

RESULTS

In current study, males (79) outnumbered females (21). The commonest mode of transmission of HIV in males was unprotected multiple heterosexual contacts, whereas in females, majority of them contracted the infection from their spouses. Fever, anorexia, lethargy, weight loss, cough, diarrhea, malaise and mouth ulcers were most common clinical presentations. TB, chronic diarrhea and oropharyngeal candidiasis were commonest opportunistic infections. Majority of the patients with opportunistic infections had a CD4 count less than 350 cells/µL. Total lymphocyte counts of 1768 cells/µL and 2354 cells/µL correlated to CD4 counts of 200 cells/µL and 350 cells/µL, respectively.

CONCLUSION

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.

KEYWORDS

HIV Infection, CD4 Count, Total Lymphocyte Count, Correlation, Opportunistic Infections.

HOW TO CITE THIS ARTICLE: Rajkondawar AV, Rodge V. Correlation between clinical profile, total lymphocytic count and CD4 count in HIV positive patients. J. Evid. Based Med. Healthc. 2017; 4(87), 5095-5098. DOI: 10.18410/jebmh/2017/1019.

BACKGROUND

Though India is a country with low HIV prevalence; it has the third highest HIV burden in the world, after South Africa and Nigeria.[1] But, over the past decade, HIV/AIDS has become a major public health problem in India.[2] 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.[3] Antiretroviral Therapy (ART) clinics were started in 2004 by the Government of India, however, there are very few published reports regarding the efficacy of the Highly Active Antiretroviral Therapy (HAART) regimens that are being used in India based on monitoring of clinical and immunological response.[4,5]

Financial or Other, Competing Interest: None.
Submission 10-10-2017, Peer Review 17-10-2017,
Acceptance 24-10-2017, Published 28-10-2017.
Corresponding Author:
Dr. Atul Vijayrao Rajkondawar,
Capitol Heights Building, Tower-1,
Flat - 1805, Jat - Tarodi, Near Medical Square,
Nagpur - 440003.
E-mail: atul.rajkondawar@gmail.com
DOI: 10.18410/jebmh/2017/1019

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However, the monitoring individuals with HIV infection/AIDS require the use of expensive tools, which are not readily available in resource-limited settings.[5] According to the WHO guidelines and CDC guidelines, a CD4 count of <200 cell/µL should be used for the initiation of ART, but high cost of CD4 count estimation in resource limited countries is a major challenge in initiating patients on Highly Active Antiretroviral Therapy (HAART).[6] Due to this, the World Health Organization (WHO) specifies that CD4 count testing is suitable, but not essential for HAART use in resource-limited settings.[7]

Therefore, in the absence of CD4 counts, Total Lymphocyte Count (TLC) <12001 rnm', though a less useful substitute, can be used for starting ART in individuals with symptomatic HIV disease. Also, necessitate the need for the evaluation and validation of the correlation of TLC with CD4 count and its usefulness as a surrogate marker for CD4 count estimation. We were going to correlate clinical profile, absolute CD4 count and TLC at <200, <350 and >350 cells/µL thresholds. The total lymphocyte count as at the time of presentation will also determine and correlated with the CD4 count at different CD4 thresholds including <200,

<350 and >350 cells/µL to establish its diagnostic utility as a surrogate marker for CD4 count.

MATERIALS AND METHODS

In this cross-sectional descriptive study, total 100 HIV positive patients of either sex, age <12 years with or without symptoms who were attended ART clinic/outpatients and inpatients at tertiary care hospital were the study group.

Exclusion Criteria

HIV positive patient less than 12 years of age. A detailed history was obtained using a pretested proforma from all the patients who were included in the study. Further, a detailed systemic examination followed by relevant investigations as mentioned in the proforma were conducted and results were noted.

Venous samples were sent for evaluation of CD4 count. Sample taken at the same time was also sent for evaluation of total leucocyte count and differential count. CD4 counts were measured by flow cytometry method. HIV infection was proved with HIV antibody detection by ELISA method. Total Lymphocyte Count (TLyC) was calculated by multiplying the Differential Count (DLC) with Total Leukocyte Count (TLC) (TLyC = TLC × DLC). Sensitivity and specificity of various total lymphocyte count cutoff were computed for CD4 count <200 cells/µL and <350 cells/µL and >350 cells/µL. We evaluated changes in total lymphocyte count as a diagnostic monitoring marker of benchmark changes in CD4 count that indicates favourable response to ART. In the patients who were symptomatic, their specimen samples like e.g. sputum, oral swab, blood, stool, urine, Cerebrospinal Fluid (CSF) and lymph node aspirate were collected as per symptoms and clinical presentations. All the specimens were collected under universal aseptic precautions in suitable sterile containers.

Statistical Analysis

Statistical software STATA version 13.1 was used for statistical analysis. Continuous variables (age, haemoglobin, total leucocyte count, total lymphocyte count and CD4 counts) presented as mean ± SD. Mean TLyC was compared with symptoms and no symptoms by performing unpaired t-test. Categorical variables (sex, symptoms and opportunistic infections) were compared by Chi-square test. Categorical variables were expressed in actual numbers and percentage. Correlation coefficient (µ) was calculated to assess the nature and the strength of relationship between CD4 counts and Hb, TLC and TLyC. P value <0.005 was considered as statistically significant.

RESULTS

Total 100 HIV positive patients were selected for the study, among them males (79) outnumbered the females (21). The mean age for males was 39.59 ± 9.38 years and for females were 34.74 ± 8.51 years. There was no overall significant difference of mean age between male and female. Table 1 show the distribution of patients in relation to risk factor. The commonest mode of transmission of HIV in males was unprotected, multiple heterosexual contacts, whereas in females, majority of them contracted the infection from their spouses.

Risk Exposure	Male	Female	Total
Sexual	75	21	**96**
Heterosexual transmission	75	11	**86**
Homosexual transmission	-	-	**-**
Spouse of HIV+	-	10	**10**
Blood Transfusion	4	-	**4**
Drug Addict	-	-	**-**

Table 1. Sex Wise Distribution of Patients in Relation to Risk Exposure

The important presenting clinical features of symptomatic patients were depicted in table 2 and table show fever, anorexia, lethargy, weight loss, cough, diarrhea, malaise and mouth ulcers were the most common clinical presentations.

Presenting Symptoms	Number	Percentage
Weight loss	52	52
Fever	71	71
Anorexia	68	68
Lethargy	40	40
Cough	39	39
Diarrhea	34	34
Malaise	20	20
Mouth ulcers	18	18
Lymphadenopathy	14	14
Genital ulcer	4	4
Skin infections	6	6
Breathlessness	3	3
Chest pain	5	5

Table 2. Distribution of Patients According to Presenting Symptoms

The common opportunistic infections were tuberculosis followed by chronic diarrhea, oropharyngeal candidiasis, pneumonitis, skin infection, genital warts and cryptococcal meningitis. Herpes zoster, pelvic inflammatory disease and pericardial effusion were other opportunistic infections seen in our study group.

CD4 Count	Number of Patients	Percentage
<100	6	6
100-200	34	34
201-350	43	43
>350	17	17

Table 3. Distribution of Patients According to CD4 Count

From, Table No. 3, it was found that the CD4 counts were less than 100/µL in 6 (6%) patients and between 101-200/µL in 34 (34%), between 201-350/µL in 43 (43%) patients and more than 350/µL in 17 (17%) patients. Majority of the patients with opportunistic infections had a CD4 count less than 350 cells/µL. The haemoglobin, total leucocyte count and total lymphocyte count were selected as study parameters to compare with the CD4 counts and were depicted in Table No. 4. The study parameters show

upward trend with CD4 counts. The total lymphocyte counts of 1768 cells/µL and 2354 cells/µL correlated to CD4 counts of 200 cells/µL and 350 cells/µL, respectively. Pearson correlation of haemoglobin, total leucocyte count and total lymphocyte count with CD4 count was 0.6446, 0.7370 and 0.3489 with p value of <0.0001, <0.0001 and 0.0004, respectively, which was highly significant.

Study Parameters Mean ± SD	CD4 Counts				P value
	<100	100-200	201-350	>350	
Haemoglobin values	7.4 ± 1.13	9.21 ± 1.50	11.44 ± 1.07	12.55 ± 1.17	<0.0001*
Total leucocytes count	3318.33 ± 357.65	4591.62 ± 981.38	6404.81 ± 600.19	9469.60 ± 2869.6	<0.0001*
Total lymphocytes count	1291.33 ± 233.1	1933.47 ± 1408.09	1858.22 ± 181.75	2508.03 ± 487.92	0.0004*

Table 4. Mean Pattern of Study Parameters with CD4 Counts

*Highly significant.

DISCUSSION

Hundred HIV positive patients were studied in our series. Among them, majority of patients (75%) were in the age group of 31-50 years. Of which, 60 were males and 15 were females with male-to-female ratio of 4:1. Our findings were almost similar to the study of NACO.[8] Also, similar to the study done by Kothari et al[9] and Sircar et al,[10] the difference in male-to-female ratio in their studies maybe due to greater rate of exposure and migration and other socioeconomic factors. Heterosexual transmission was the commonest mode of spread of HIV infection in our study population, which was like to the findings in other studies.[9-11] This was because multiple unprotected sexual contacts are the commonest mode of disease transmission in India. But, the study conducted by American College of Physicians and Infectious Diseases Society of America[12] has accounted sexual contact among homosexual men as well as intravenous drug abuse for most of the cases. This may be accounted by the differences in the sociocultural perceptions and practices between the two regions. There were only 4 (4%) patients who presented with a history of blood transfusion in our study. This was compared with study of Sircar et al.[10]

Fever, anorexia, weight loss, lethargy, cough, diarrhea, malaise, mouth ulcers and lymphadenopathy were the commonest clinical manifestations and which were consistent with findings of Kothari et al[9] and Sircar et al.[10] Tuberculosis was the most common opportunistic infection present in 57 (57%) patients. Among them, 27 (27%) had pulmonary tuberculosis, 22 (22%) had extrapulmonary tuberculosis and 8 (8%) had both pulmonary and extrapulmonary tuberculosis. This finding was correlated with the study of Sharma et al.[11] Chronic diarrhea was the second commonest infection present in 34 (34%) patients and the causative organism was identified to be either Giardia lamblia or Entamoeba histolytica in 6 patients. Chronic diarrhea due to Entamoeba histolytica was due to coexisting infection. In the others, the causative organism could not be identified. Oropharyngeal candidiasis was present in 18 (18%), followed by pneumonitis in 8 (8%) patients. All suspected patients of pneumonitis were screened for pneumocystis carinii, but was not detected even Mycobacterium avium-intracellulare could not be detected. Opportunistic skin infections such as molluscum contagiosum and fungal infections were seen in 6 (6%) patients. 2 (2%) patients each had pericardial effusion and 2 (2%) patient pelvic inflammatory disease.

The CD4 counts were less than 200 cells/µL in 40 (40%) of the patients in our study. There was a significant relationship between CD4 count and the presence of TB as the CD4 counts varied from less than 100 cells/µL to greater than 500 cells/µL. As the CD4 count declines, incidence of extrapulmonary tuberculosis increases over pulmonary tuberculosis. According to current medical scene, the risk of developing pneumococcal and other bacterial pneumonias, pulmonary TB, herpes zoster, candidiasis, Kaposi's sarcoma is high with a CD4 count more than 200-500 cells/µL and the pneumocystis carinii pneumonia, disseminated herpes simplex, toxoplasmosis, cryptococcosis, miliary and extrapulmonary tuberculosis and oropharyngeal candidiasis with a CD4 count less than 200 cells/µL and disseminated cytomegalovirus infection and mycobacterium avium complex infection with a CD4 count less than 50 cells/µL.

In current study, the total leucocyte count and total lymphocyte count were showing positive trend to CD4 counts and were statistically significant. The total leucocyte counts of 5788 cells/µL and 8736 cells/µL showed similar observations to CD4 counts of 200 cells/µL and 350 cells/µL. Total lymphocyte counts of 1768 cells/µL and 2354 cells/µL showed similar observations to CD4 counts of 200 cells/µL and 350 cells/µL, respectively. The P value was highly significant with Pearson correlation of 0.7370 for total leucocyte counts (P value <0.0001) and 0.3489 for total lymphocyte count (P value <0.0004). Our findings were compared with previous studies.[13-16] Apart from these studies, Post et al[17] also studied the utility of CD4 counts and total lymphocyte counts as predictors of HIV disease progression and concluded that for each clinical stage a significant difference in the progression to AIDS and mortality was predicted by total lymphocyte count above or below 1250 cells/µL. Survival and progression to AIDS occurred at similar rates in patients with total lymphocyte count of 1250 cells/µL. The pattern of CD4 counts overtime is more important than any single CD4 count value. CD4 counts generally decrease as HIV progresses. Therefore, it is more valuable to evaluate a series of CD4 counts than any single CD4 count. As the CD4 count is affected by the time of the day (lower in the morning), in acute illnesses,

refrigeration of the blood sample (decreased CD4 count) with rough handling or contamination of blood sample, so the serial recording of total lymphocyte count can give an equally stable reflection of progression of disease and development of AIDS in HIV infected persons. It becomes more feasible especially in developing countries as CD4 count costs around 30 US dollars while total lymphocyte counts cost around 2.4 US Dollars. Monitoring the patients with total lymphocyte count has an enormous cost benefit in patients living in resource limited countries. The cost of TLyC and DLC in standardised laboratories in India is Rs. 150 and CD4 count is Rs. 1850.

CONCLUSION

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.

Acknowledgement

The authors would like to thank the Department of Medicine and Administration of Government Medical College, Nagpur, Maharashtra, for permission to study and providing facility to carry out the work.

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