A PROFILE OF HUMAN IMMUNODEFFICIENCY VIRUS INFECTED PATIENTS IN YENEPLOYA MEDICAL COLLEGE HOSPITAL WITH SPECIAL REFERENCE TO CORRELATION BETWEEN CD4 COUNT AND TOTAL LYMPHOCYTE COUNT

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HOW TO CITE THIS ARTICLE:

Sajid Chalihadan, Mohammed Kunhi, C.P. Abdul Rahman. "A Profile of Human Immunodeficiency Virus infected patients in Yeneploya Medical College Hospital with special reference to Correlation between CD4 Count and total Lymphocyte Count". Journal of Evolution of Medical and Dental Sciences 2013; Vol. 2, Issue 52, December 30; Page: 10204-10227.

ABSTRACT: BACKGROUND AND OBJECTIVES: To study the clinical presentation, spectrum of systemic involvement, opportunistic infections and the correlation between CD4 + cell count and TLC for monitoring disease progression in HIV patients. Previous studies have shown that TLC is an inexpensive and useful tool for monitoring HIV progression. **METHODS:** This was a 2 year prospective study in which cases were examined and according to the proforma, TLC and CD4+ counts were assessed in 50 HIV positive patients who attended Yeneploya Medical College Hospital, Mangalore between October 2005 and September 2007. Sensitivity and specificity of various TLC cut-off were computed for CD4 count <200 cells/mm³ and statistical indices computed. Pearson's correlation coefficient was used to find out the correlation between CD4+ count and TLC at baseline. **RESULTS:** 45 male and 5 female patients, having mean age of 38.08± 9.01 years (range 20 – 60 years) were studied. 70% were in 20-40 years age group. 34% were related to transport services. Heterosexual mode of transmission was seen in 64%, commonest presenting symptoms were fever and weight loss, oral candidiasis was present in 26% and lymphadenopathy in 46% of subjects. Tuberculosis was the most common opportunistic infection seen in 68% of subjects. One patient had AIDS dementia complex, one had HIV nephropathy and in 1 and a presumptive diagnosis of Kaposi's sarcoma was made. Tubercular meningitis was the most common neurological manifestation. The mean baseline CD4+ count in study group was 175 cells/mm³. The mean baseline TLC was 1338 cells/mm³. The scatter diagram shows, as the CD4 T cells rise, the TLC level also rises. The sensitivity and specificity of TLC < 1200 and CD4 count <200 was 91% and 53% respectively with a positive predictive value of 70% (p = 0.0001). **CONCLUSION:** Occupation was the important risk factor for HIV transmission and heterosexual contact is the commonest mode of spread. Among opportunistic infections, tuberculosis was most common. There was a definite correlation between the TLC and CD4 count in HIV positive patients before treatment. It is evident from this study that TLC can be used in place of CD4+ T cell counts in resource-limited settings to monitor the disease progression.

INTRODUCTION: The world wide epidemic of Human Immunodeficiency Virus (HIV) is an international health problem of extraordinary scope and unprecedented urgency¹. Since 1980 till today HIV epidemic has continued its dramatic expansion universally, both geographically and in terms of risk groups. The epidemiological scenario is also changing, from a disease mainly of homosexual males to a rapidly growing population of HIV infected females, children and men who

are not homosexuals. The spectrum of HIV infection includes asymptomatic cases to AIDS at other extreme. The diagnosis rests on clinical manifestations and laboratory markers.

In India, the socioeconomic and cultural environment is important in disease transmission and prevalence, as also the clinical spectrum is very different from western society. One of the purposes of this study was to know the different patterns of clinical presentation of HIV infection in this region

Soon after HIV was found to be the cause of AIDS, it was shown that the virus binds to receptors on CD4 cells, enters the cells, and uses them to create new virus, destroying them in the process. This results in the depletion of CD4 cells and immunodeficiency.²

With the increased availability of equipment to perform CD4 counts and the knowledge that CD4 cells were the primary target of HIV, the determination of CD4 count became the standard measure of immunodeficiency in adult HIV-infected patients in resource-rich countries. The relative ease of CD4 cell monitoring also led to its advocacy in treatment guidelines for determining when to start, stop, or change ART and for deciding when to initiate prophylaxis for opportunistic infections (OIs). This is despite the fact that CD4 count does not always correlate with functional immunity; some patients with normal CD4 counts are susceptible to OIs and some patients with significantly depressed CD4 counts do not seem unduly susceptible to OIs.

The determination of CD4 cell count and percentage is too expensive for most health facilities in resource-poor countries like India to perform routinely³. In contrast, TLC can be derived easily in resource-poor countries by performing a routine white blood cell count. TLC is the total white blood cell count multiplied by the lymphocyte percentage; for example, a total white blood cell count of 6,000 cells / μL with a lymphocyte percentage of 30% would result in a TLC of 1,800 cells / μL ³. The equipment and skills to perform total white blood cell count and differential are readily available in most hospitals and clinics in resource-poor countries. The need to rapidly expand the use of ART in resource-poor countries as well as the human resource constraints, cost, and infrastructure concerns surrounding CD4 cell measurements have prompted to evaluate the utility and predictability of TLC as a measure of immune function and its usefulness in guiding initiation of ART. This study also attempts to correlate CD4 count with TLC

MATERIALS AND METHODS

Design: Prospective study of 2yrs from October 2005 to October 2007.

Setting: Yenepoya Medical College & Hospital

1. **Inclusion Criteria:** Adult HIV positive patients above 16 yrs with a definite diagnosis of HIV illness by CDC revised surveillance.

2. **Exclusion Criteria**

1. Pediatric HIV positive patients.
2. Patients on immunosuppressant therapy.
3. Patients who are diagnosed as HIV positive earlier and on treatment for the same.

Patient Enrollment and Monitoring: 50 cases of HIV positive patients were recruited from all treating units at Yenepoya Medical College Hospital from October 2005 to October 2007.

These patients were also treated for opportunistic infections.

Method of collection of Data: Diagnosis of HIV was made in these patients by Detailed clinical history and physical examination.

Routine laboratory investigations including Elisa(2 ELISA).

Venous samples were sent for evaluation of CD4 count (by Flow cytometric method). At the same time samples were sent for evaluation of TLC.

Total lymphocyte count (TLC) was calculated by multiplying the differential lymphocyte count with the total leucocyte count. [TLC=Total leucocyte countx Differential lymphocyte count]

In the patients who were symptomatic, the following investigations were done.

Collection and processing of specimens: Various samples e.g. sputum, oral swab, blood, stool, urine, cerebrospinal fluids (CSF), lymph node aspirate were collected as per symptoms and clinical presentations. All the specimens were collected under universal aseptic precautions in suitable sterile containers.

Oral swab: Oral swabs were collected in cases presenting with oral thrush. Two sterile swabs were taken and each rubbed against the right tonsil and rolled along the soft palate to the left tonsil. Curdy white patches were also swabbed. Gram staining was done with one swab and the other swab was streaked on Sabouraud's dextrose agar slope. Germ tube test was also performed for presumptive identification of *Candida albicans*.

Stool: Fresh samples of stool were collected in sterile, dry, leak proof, wide-mouthed container.

Wet mount- Direct saline mounts and iodine mounts were screened under microscope for helminth eggs, larvae, protozoan cysts, trophozoites, pus cells and possible fungal elements. After concentration method supernatants were discarded, sediment was used for Kinyoun cold test for detection of oocysts of *Cryptosporidium*, *Cyclospora*, *Isospora* and *Sarcocystis*.

Sputum: Early morning sputum was collected in a wide mouthed sterile container. Instructions were given to rinse the mouth with tap water before sample collection, and to collect expectoration and not saliva.

Wet mount- sputum sample was taken on a clean glass slide and 2 drops of 10% KOH was added and covered with a cover slip. Slip was kept in incubator at 37°C for 10 mins and examined for fungal elements.

Staining of sputum was done for detection of

- Gram stain- to see pyogenic bacteria, pus cells and epithelial cells
- Ziehl- Neelsen stain for acid fast bacilli
- Methanamine silver nitrate stain- for the detection of *Pneumocystis carinii* cysts

Urine: Mid-stream urine samples were collected in sterile container. All the samples were processed within one hour of collection. Gram stain was done to detect pus cells, epithelial cells, bacteria and yeast cells.

Cerebrospinal fluid (CSF): CSF samples were obtained by lumbar puncture and processed immediately. CSF fluid was sent to microbiology for

- Culture
- Staining- gram stain, Ziehl-Neelsen's stain and methylene blue stains were used to detect different pathogens
- India ink wet mount- it was done to detect presence of *Cryptococcus*.

Blood: Skin at the site of venipuncture was cleaned with 70% alcohol followed by 2% tincture iodine. Total 15ml blood was collected from each patient. 10ml was used for blood culture and 5ml was collected in sterile penicillin vial for serological tests.

Serology: The blood collected in penicillin vial was allowed to clot. Samples were centrifuged and serum was collected for following tests

- VDRL
- HbsAg
- HCV

Method of Statistical Analysis: Sensitivity and specificity of various total lymphocyte count cut offs were computed for CD4 count <200 cells/mm³. Correlated and statistical indices computed for all patients.

Sensitivity, Specificity, Positive Predictive value and Negative Predictive value: TLC values at 1200 or less, compared with CD4 values at <200, then the number of patients with True Positive (TP), False Positive (FP), True Negative (TN) and False Negative (FN) were determined. The following were calculated:

Sensitivity: $[TP / (TP+FN)]$

Specificity: $[TN / (TN+FN)]$

Positive Predictive Value: $PPV = [TP / (TP+FN)]$

Negative Predictive Value: $NPV = [TN / (FN+TN)]$

In the above test P value less than 0.05 were taken to be statistically significant. The data was analyzed using Statistical Package for Social Science (SPSS) package.

RESULTS AND ANALYSIS: A total number of 50 cases of HIV infected patients admitted in Yenepoya Medical College Hospital, Mangalore who met the inclusion criteria were studied.

1. AGE AND SEX DISTRIBUTION:

Age in years	Male	Female	Total
<20	-	-	-
21-30	12	1	13
31-40	20	2	22
41-50	10	2	12
51-60	2	-	2
>61	1	-	1

Table No. 1: The age and sex distribution

Out of the 50 cases studied, 45 (90%) were males and the remainder 5 (10%) were females. Their ages ranged from 20 years to 60 years with a mean of 38.08 ± 9.01 . The ratio of Male: Female was 9: 1. The maximum incidence of 70% was seen in the age group between 20 to 40 years, of which 91.42% (32/35) were males. (Table. 1, Fig 1)

FIGURE No: 1

2. OCCUPATION:

	Male	Female	Total
Transport	17	-	17
Farmers	5	-	5
Hotel workers	11	-	-
Laborers	7	1	8
Others	5	4	9

Table No. 2: Sex wise distribution of different types of occupations

Out of the 50 cases studied, 34% (17/50) were in transport, 22% (11/50) were hotel workers, 16% (8/50) were laborers, and the rest constituted farmers, businessmen, housewives.(Table.2, Fig 2)

Fig. 2: Distribution of types of occupation

3. MODE OF TRANSMISSION:

Out of 50 cases, 64% (32/50) had heterosexual (multiple sexual partners), Homosexual 10% (5/50), Blood transfusion 0.5% (1/50) and mode of transmission and history could not be obtained in 24% (12/50). (Fig 3).

Fig. 3: Distribution of Mode of Transmission

4. DURATION SINCE TIME OF FIRST RISK EXPOSURE:Duration since time of first risk exposure ranged from 2 years to 20 years with the mean of 8.27 ± 4.181 .

5. PRESENTING SYMPTOMS

Presenting symptoms	Male	Female	Total
Fever > 1 month	36	4	40
Cough	27	2	29
Diarrhea> 1 month	9	2	11
Significant weight loss	39	3	42
Abdominal pain	10	-	10
Headache	5	1	6
Seizures	3	-	3
Altered sensorium	2	0	2
Dysphagia	1	1	2
Ear discharge.	1	-	1

Table No. 3: Sex wise distribution of presenting symptoms

Out of 50 cases, most common presenting symptoms were fever of more than 1 month in 80% (40/50) and significant weight loss in 84% (42/50), 58% (29/50) had cough out of which 40% (20/50) had expectoration. 22% (11/50) had diarrhea of more than 1 month. Pain in abdomen was complained by 20% (10/50) of patients, 12% (6/50) had headache and 6% (3/50) had seizures of generalized tonic clonic type. Two patients presented with altered sensorium and two with dysphagia. Purulent discharge from the ear was complained by one patient. (Table.3, Fig 4).

Fig. 4

6. CLINICAL SIGNS

Signs	Male	Female	Total
Lymphadenopathy	17	3	20
Oral candidiasis	10	3	13
Skin lesions	7	0	7

Table No. 4: Sex wise distribution of clinical signs

Of the total number of patients studied on general physical examination, 40% (20/50) had palpable lymphnodes, 26% (13/50) had oral candidiasis, 14% (7/50) had skin manifestations and commonest manifestation was papular eruption seen in 42.85% (3/7) of cases, seborrheic dermatitis, hypopigmented macules, penile ulcer were seen in 57.16% (4/7) cases. (Table 4, Fig 5).

Fig. 5

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7.LABORATORY PROFILE:Hemoglobinestimation was done in 50 cases. 14% (7/50) had hemoglobin of less than 8gm% and 26% (13/50) had hemoglobin of more than 12gm% with mean of 10.42 ± 1.99 . Peripheralsmear in 62%ofcaseswerenormocytic normochromic type. (Table 5, Fig 6).

Hemoglobin in gm.%	Male	Female	Total
<8	4	3	7
8 – 10	16	1	17
10 – 12	12	1	13
>12	13	-	13

Table No. 5: Sex wise Distribution of Hemoglobin Levels

Fig. 6: Distribution of Himoglobin levels

Peripheral smear	Male	Female	Total
Microcytic hypochromic	14	2	16
NormocyticNormochromic	28	3	31
Normocytic hypochromic	0	0	0
Dimorphic	2	0	2
Thrombocytopenia	1	0	1

Table No. 6: Sex wise distribution of peripheral smear study

TLCvs.CD4+COUNT: The overall mean baseline CD4+ counts in study group was 175 cells/mm³ while the overall mean baseline Total Lymphocyte count (TLC) in study groupwas 1338 cells/mm³.There is a fair positive correlation between CD4 count and TLC ($r = 0.55$, $p = <0.0001$). (Table 7, Fig 7)

	TLC
CD4	$r: 0.55$ $p: <0.0001$

Table No. 7: Pearson Partial Correlation Coefficient

Fig. 7: Scatter plot of CD4+ counts vs TLC

TLC			<1200	>1200	Total
CD4	<200	No	20	13	33
		%	60.61%	39.39%	
CD4	>200	No	2	15	17
		%	11.76%	88.24%	
Total		No.	22	28	50

Table No. 8: CD4+ Count < 200 vs. TLC < 1200

When patients with CD4 count of <200 cells/mm³ and TLC of <1200 cells/mm³ were correlated, the results showed a highly significant statistical correlation ($P < 0.001$) with sensitivity of 91% and specificity of 53% and positive predictive value of 70% and negative predictive value of 30%.

CHESTX - RAY:

Type of lesion	Male %	Female %	Total %
Upper zone lesions	17.8	0	17.8
B/L infiltrations	39.28	7.14	46.42
Lower zone lesion	10.71	0	10.71
Pleural effusion	7.1	3.61	10.71
Pneumothorax	3.57	0	3.57
Cardiomegaly	3.57	0	3.57
Miliary mottling	7.14	0	7.14

Table No. 9: Sex wise distribution of various chest X-ray patterns

Out of 50 patients studied, 28 had radiological abnormalities. There were apical lesions in 5, bilateral extensive infiltrations in 13, cardiomegaly in 1, pleural effusion in 3, lower lobe opacities in 3, pneumothorax in 1 and miliary mottling in 2. (Table 9, Fig 8))

Fig. 8

Opportunisticinfections and other associated conditions in HIV infected patients

Tuberculosis:Out of 50 cases studied, tuberculosis was the commonest opportunistic infection with 68% (34/50) of cases having tuberculosis. 38.23% (13/34) had only pulmonary tuberculosis, 38.23% (13/34) had only extra pulmonary tuberculosis and 23.53% (8/34) had both pulmonary and extra pulmonary tuberculosis. (Fig 9).

Fig. 9: Distribution of types of Tuberculosis

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Secondary Infections: Out of 50 cases, 6% (3/50) had secondary bacterial non opportunistic infections, out of which 2 were pneumonia caused by gram negative bacilli and 1 was of chronic suppurative otitis media.

Neurological manifestations: Out of 50 cases, 28% (14/50) had neurological manifestations. Out of them 50% (7/14) had tubercular meningitis, 14.28% (2/14) had tuberculoma, 14.28% (2/14) had tubercular arachnoiditis presenting with myeloradiculopathy. 1 patient was diagnosed to have HIV encephalopathy (AIDS dementia complex) and 2 patients had progressive multifocal leukoencephalopathy. (Fig 10).

Fig. 10

Sexually transmitted diseases: One patient i.e. 2% (1/50) had gonorrhea and one patient was diagnosed to have hepatitis B.

Persistent generalized lymphadenopathy was found in one out of 50 cases studied.

Renal manifestation: Out of 50 cases studied, one patient had HIV associated nephropathy and one patient had chronic renal failure.

Malignancy: Out of 50 cases studied, one patient had Non-Hodgkin's lymphoma and in one patient probable diagnosis of Kaposi's sarcoma was made.

Fever of Unknown Origin: Out of 50 patients, 80% (40/50) had fever of more than 1 month duration, of which definitive diagnosis could not be made in 3 cases and were diagnosed as fever of unknown origin.

Parameter	Percentage of cases
Tuberculosis	68
Pulmonary	20
Extra-pulmonary	38
Both	10
Secondary bacterial infections	6
Neurological symptoms	28

Tubercular meningitis	50
Tuberculoma	14.28
TB arachnoiditis	14.28
AIDS dementia	7.14
Progressive multifocal leucoencephalopathy	14.28
Sexually transmitted diseases	4
Gonorrhea	2
Hepatitis B	2
Renal Manifestations	4
HIV associated nephropathy	2
Chronic renal failure	2
Fever of unknown origin	6
Malignancy	4
Non-Hodgkin's lymphoma	2
?Kaposi's Sarcoma	2
Persistent generalized Lymphadenopathy	2

Table No. 10: Distribution of various opportunistic Infections and other manifestations.

DISCUSSION: The observations made in 50 cases of HIV infected patients admitted to YenepoyaMedicalCollegeHospital, Mangalore between October 2005 to September 2007, are discussed and compared with other studies.

1. AGE AND SEX: Ghate M.V et al⁴ in his study on changing trends in clinical presentation of HIV infected persons in Pune found that 88.1% of the cases were in the age group between 21 years and 40 years and it was the male population that was more affected as compared to the females with male to female ratio of 2.22:1.

Study done by Kothari K et al⁵ in 2001 showed that 90% of the cases were in the age group of 20 to 40 years and male population constituted 83.33% with male to female ratio of 5: 1. In a study done by Mandal A.K et al⁶, 81.16% of cases were in the age group of 20 to 40 years with male to female ratio of 1.5: 1.

The age of the patients in the present study ranged from 20 to 61 years with 90% males and 10% females with a male to female ratio of 9:1.

The incidence of maximum number of HIV infected cases in the age group of 20 to 40 is comparable with other studies.

This finding of male preponderance is comparable with other studies that the incidence of HIV infection is more common in males than females. This data suggests that sexually active population is more affected.

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The comparable studies are shown in a tabular column below

Study series	Total number of patients	Males in %	Females in %	M:F	21- 40 years in%
Mandal A.K ⁶ et al (2000)	88	60.87	39.13	1.5:1	81.16
Kothari K ⁵ et al (2001)	30	83.33	16.66	5:1	90
Ghate M.V ⁴ et al (2002)	2801	68.97	31.02	2.22:1	88.1
Present study	50	90	10	9:1	70

2. Occupation: Mandal A.K⁶ et al in his study found that the main risk groups were truck drivers and laborers. Study done by Kothari K et al⁵ showed that major risk group was people in transport services constituting 40% of all cases.

In the present study people in transport services constituted 34% of all cases and Hotel workers constituted 22% of all cases.

This finding is comparable with other studies that the incidence of HIV infection was high among people working in transport probably because of longer duration of stay away from the family.

Occupation	Mandal AK et al ⁶ al (2000 in %)	Kothari k et al ⁵ al (2001 in %)	Present Study (%)
Transport	11.36	40	34
Laborer	17.05	20	16
Farmers	-	16.67	10
Hotel worker	-	-	22
Female sex worker	10.22	-	-
Others	61.36	23.33	18

4. Mode of transmission: John T.J et al⁷ in his study showed that 90% of the patients had multiple sex partners and heterosexual route was the major mode of transmission.

Rajasekaran Set al⁸ showed heterosexual promiscuity in 74.4% of patients. Of the remaining, 15.38% were females who had acquired the infection through their HIV infected husbands while remaining 10.25% constituted commercial sex workers and intravenous drug abusers.

Kothari Ket al⁵ in his study showed that heterosexuality accounted for 90% of the total cases.

In this study, heterosexual mode of transmission was the major mode of transmission in 64%; 10% showed homosexual and in the remaining 24% of the cases reliable history could not be elicited.

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This finding is not comparable with other studies.

4. Presenting symptoms: A study of common presenting symptoms and signs was made. We noted that fever and weight loss were the most common presenting symptoms constituting 80% and 84% of cases respectively. This finding is comparable with other studies done by Colebunders R et al⁹, showed fever and weight loss in 21.83% and 29.31%, Lakshmi V. et al¹⁰ in 61% and 45%, Kothari K et al⁵ in 96% and 66% of cases. Then next common symptom in our study was cough > 1 month in 58% of cases which was comparable with study done by Kothari K et al⁵ who showed cough > 1 month in 60% of cases. However in studies done by Colebunders R et al⁹ and Lakshmi V et al¹⁰, only 15.5% and 11% of cases had cough respectively.

We see that present study has reported a higher incidence of cough > 1 month as compared to the two above mentioned studies. This could be explained by higher incidence of tuberculosis in the present study.

Next common symptom reported in the present study was diarrhea > 1 month, in 22% of cases. This finding is comparable with studies done by Lakshmi V et al¹⁰ and Kothari K et al⁵ which showed an incidence of 23% in both the studies.

However in a study done by Colebunders R the above mentioned symptom was seen in only 9.77% of cases, which is lower incidence compared to the present study.

Pain abdomen was seen in 20% of cases in the present study. However Lakshmi V et al¹⁰ reported in 9% of cases and Kothari K et al⁵ in 6.6% of cases.

This study showed a higher incidence of this symptom compared to the above mentioned studies.

Altered sensorium was seen in 4% of cases in present study. Kothari K et al⁵ reported the same in 26% of cases. The present study had recorded a lower incidence as compared to the study done by Kothari K et al, probably due to the small study population in our study when compared to the other.

Dysphagia was seen in 4% of cases in the present study. However Kothari K et al⁵ reported in 30% of cases.

The table showing the comparable studies is given below

	Colebunder R et al⁹ (1987) %	Lakshmi V et al¹⁰ (1998) %	Kothari K et al⁵ (2001)	Present Study %
Fever > 1 month	21.83	61	96	80
Weight loss > 10%	29.31	45	66	84
Cough > 1 month	15.51	11	60	58
Diarrhea > 1 month	9.77	23	23	22
Pain abdomen	-	9	6.6	20
Altered sensorium	-	-	26	4
Dysphagia	-	-	30	4

5. Clinical findings in general examination: The present study showed that skin lesions were present in 12% of patients, oral candidiasis in 26%, significant lymphadenopathy in 40% and genital ulcer in 2% of cases. Much lower incidence were reported in studies by Colebunders R et al⁹, who

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reported skin lesions in 4.02%, oral candidiasis in 9.77%, lymphadenopathy in 7.47% and genital ulcer in 2.87%. Lakshmi V et al¹⁰ reported oral candidiasis in 6%, lymphadenopathy in 6% and genital ulcer in 5% of cases. However Kothari K et al⁵ reported a much higher incidence of skin lesions in 33%, oral candidiasis in 70%, lymphadenopathy in 43% and genital ulcers in 23% of patients.

The table showing comparable studies is given below.

Study Series	Skin Lesions %	Oral candidiasis %	Lymphadenopathy %	Genital Ulcer%
Colebunders R et al ⁹ (1987)	4.02	9.77	7.47	2.87
Lakshmi V et al ¹⁰ (1998)	-	6	6	5
Kothari K et al ⁵ (2001)	33	70	43	23
Present study	12	26	40	2

Opportunistic infections and other associated conditions in HIV infected cases:

a. Tuberculosis: In the present study most common opportunistic infection was tuberculosis with an incidence of 68%. 38.23% had only pulmonary tuberculosis, 38.23% had only extrapulmonary tuberculosis and 23.54% had both pulmonary and extra pulmonary tuberculosis. However much higher incidence of pulmonary tuberculosis and lower incidence of extra pulmonary tuberculosis was shown by other studies done by Hira S.K et al¹¹ who reported 65.34% pulmonary, 27.84% extra pulmonary and 6.82% both pulmonary and extra pulmonary tuberculosis. Rajasekaran S et al⁸ showed 55.6% of pulmonary tuberculosis and 30.5% combined disease. Zuber Ahmed et al¹² showed 74.7% pulmonary tuberculosis, 19.8% extra pulmonary tuberculosis and 5.5% combined disease. However Chacko S et al¹³ reported a lower incidence of pulmonary tuberculosis of 30% and higher incidence of combined disease with 48% and extra pulmonary tuberculosis constituting 22%, when compared to above mentioned studies.

The comparable studies are given below:

Tuberculosis	Chacko S et al ¹³ (1995) %	Hira S.K ¹¹ et al(1998) %	Rajasekaran S ⁸ et al (2000)%	Zuber Ahmed et al ¹² (2003) %	Present Study
Pulmonary	30	65.34	55.6	74.7	38.23
Extra pulmonary	22	27.84	13.9	19.8	38.23
Combined*	48	6.82	30.5	5.5	23.54

* Both pulmonary and extrapulmonary

Chest X-ray Findings and HIV infection: In the present study, 28 patients showed radiological abnormalities with upper zone lesions in 17.8%, B/L infiltrations in 46.42%, lower zone lesions in 10.71%, pleural effusion in 10.71%, pneumothorax in 3.57%, miliary shadow in 7.14%

and cardiomegaly in 3.57%. These findings were comparable with other studies done by Chacko S et al¹³ who reported upper zone lesions in 26.92%, B/L infiltrations in 23.07%, lower zone lesions in 7.69%, pleural effusion in 15.38%, pneumothorax in 3.84%, military shadows in 3.84% and hilar adenopathy in 19.23%.

Arora et al¹⁴ reported upper zone lesions in 17.65%, B/L infiltrations in 29.42%, lower zone lesions 11.75%, pleural effusion in 17.65%, military shadows in 5.89% and hilar adenopathy in 17.65%.

However Agarwal et al¹⁵ reported a higher incidence of typical upper zone lesions in 57.1%, B/L infiltrations in 28.5% and lower zone lesions in 14.3% of cases.

A table showing comparable study is given below:

Radiological lesions	Arora et al¹⁴ (1993) %	Chacko S et al¹³ (1995)	Aggarwal S.K et al¹⁵ (2003)	Present Study
Upper zone lesions	17.65	26.92	57.1	17.8
B/L infiltrations	29.41	23.07	28.5	46.42
Lower zone lesions	11.75	7.69	14.3	10.71
Pleural effusion	17.65	15.38	-	10.71
Pneumothorax	-	3.84	-	3.57
Military shadows	5.89	3.84	-	7.14
Any other	B/L hilar adenopathy 17.65	B/L hilar adenopathy 19.23	-	Cardiomegaly 3.57

Neurological manifestations in HIV disease: In the present study, 28% of patients had neurological complications. Of these, 50% of patients had meningitis with all the cases being tubercular meningitis. We did not have any patients with cryptococcal meningitis. However studies done by Lakshmi et al¹⁰ reported meningitis in 70.59% of cases with 76.16% of them being tubercular, cryptococcal meningitis in 12.5% of cases and syphilitic meningitis in 8.33% of cases.

Sircar AR et al¹⁶ reported meningitis in 58.33% of cases with tubercular meningitis in 42.86% of cases and cryptococcal meningitis in 57.14%.

Wadia R.S et al¹⁷ reported meningitis in only 17.88% of cases with majority of them being cryptococcal in etiology constituting 67.44% of the total meningitis cases. Tubercular meningitis was seen in 18.6%, aseptic meningitis in 4.65%, pyogenic meningitis in 5.81%, syphilitic in 2.32% and both cryptococcal and tubercular meningitis in 1.16%.

The above two mentioned studies reported much higher incidence of cryptococcal meningitis when compared to the present study. This could be explained by very large sample size in those studies.

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The present study showed tuberculoma in 14.28% of cases, spinal cord involvement in the form of myelo radiculopathy in 14.28%, AIDS dementia complex in 7.14% and progressive multifocal leuko encephalopathy in 14.28%.

However the other studies had not reported any cases of progressive multifocal leuko encephalopathy or muscular dystrophies or myopathies.

Lakshmi et al¹⁰ had reported tuberculoma in 5.88% of cases, myelo radiculopathy in 5.88% of cases and toxoplasma infection in 17.65% in contrast to the present study where we did not find toxoplasma infection affecting central nervous system in any case.

Sircar AR et al¹⁶ reported AIDS Dementia complex in 16.67% of cases and sensori motor neuropathy in 25% of cases.

Wadia RS et al¹⁷ reported myelopathy in 4.36% of cases, ADC in 4.36%, neuropathies in 28.27% of cases and cranial neuropathies, seizures-, headache strokes, altered sensorium, meningism constituted 45.13% of cases.

However present study did not report any neuropathies in comparison to the above two studies.

The table showing the comparable studies is given below:

	Lakshmi et al ¹⁰ (1998)	Sircar AR et al ¹⁶ (1998)	Wadia R.S et al ¹⁷ (2001)	Present Study
Meningitis	70.59	58.33	17.88	50
a. Tubercular	79.16	42.86	18.6	100
b. Cryptococcal	12.5	57.14	67.44	-
c. Aseptic	-	-	4.65	-
d. Pyogenic	-	-	5.81	-
e. Syphilitic	8.33	-	2.32	-
f. Combined	-	-	1.16	-
Tuberculoma	5.88	-	-	14.28
Myelopathy/Myelodradiculopathy	5.88	-	4.36	14.28
AIDS Dementia Complex	-	16.67	-	7.14
Progressive Multifocal Leukoencephalopathy	-	-	-	14.28
Any other	Toxoplasma- 17.65	Neuropathy - 25%	Neuropathy- 29.27% Others -45.13	-

Sexually transmitted diseases (STD) and HIV: The present study reported one patient having Hepatitis B and one patient with genital gonorrhea constituting 2% each of total cases. This finding is comparable with study done by Lakshmi et al¹⁰ which reported Hepatitis B in 2.3% of cases and Syphilis in 0.5% of cases. However much higher incidence of STDs was reported by Shah H et al¹⁸ who showed presence of syphilis in 10% of cases, Chancroid in 10%, Herpes genitalis in 15%, Condyloma acuminata in 10%, balanoposthitis in 30%, Candidial vaginitis in 15% and nonspecific urethritis in 10% of cases.

Sayal SK et al¹⁹ reported chancroid in 32.5%, syphilis in 23%, LGV in 11.9%, gonorrhea in 2.6% and herpes genitalis in 3.2% cases.

This higher incidence of STD could be explained because their study was conducted in patients attending STD clinics.

Secondary bacterial infections and HIV: In the present study, out of 50 cases, 2 cases had pneumonia caused by gram negative bacilli and 1 patient had chronic suppurative otitis media.

However in a study done by Kothari K et al⁵ reported secondary infections in 7 patients (7/30) out of which 3 had pneumonia, 2 had lung abscess, 1 case had pyogenic meningitis and 1 had acute suppurative otitis media. Chacko S et al¹³ reported 18 cases of secondary infection with 11 cases of pneumonia, 3 had urinary tract infection, 2 had enteric fever, 1 borderline lepromatous leprosy and 1 had gastroenteritis due to *Shigella* *Sonnei*.

The present study reported lesser incidence of secondary bacterial infections when compared to the above mentioned studies.

Persistent Generalised Lymphadenopathy (PGL): The present study reported PGL in 2% of cases which was much lower when compared to studies done by Kothari K et al⁵ who reported PGL in 20% of cases and Sircar¹⁶ et al in 22.5% of cases.

Renal involvement and HIV: The present study reported 1 (2%) case of chronic renal failure and 1 (2%) case of HIV associated nephropathy. This finding is comparable with the study done by Kothari K et al⁵ who reported HIV associated nephropathy in 3.3% of cases and renal involvement in the form of albuminuria and hematuria in 7% of cases.

Malignancies and HIV: The present study reported 1 case of Non-Hodgkin's lymphoma and 1 case of suspected Kaposi's sarcoma which is comparable with other studies done by Kothari K⁵ et al who reported 1 case of Non-Hodgkin's lymphoma.

Chacko S et al¹³ reported 1 case of Non-Hodgkin's lymphoma and 2 suspected lymphomas where definitive diagnosis could not be done because of lack of facilities.

In many resource poor countries, clinicians are severely limited in the use of standard of care assays to help determine disease progression in HIV positive patients. This limitation can result in a potentially dangerous postponement of the initiation of antiretroviral therapy¹⁹⁻²⁶ Previous studies had shown that TLC is a low cost and useful tool for monitoring HIV progression and triggering Opportunistic infection prophylaxis in resource poor settings.

In this setting WHO recommends using the total lymphocyte count (TLC) as a surrogate marker for the CD4 T cell count. If the CD4 lymphocyte count is not available, WHO recommends initiating HAART in WHO stage II and III disease when accompanied by a TLC of less than 1200 cells/mm³.

Depletion of CD4+ T cells is one of the hallmarks of progression of HIV-1 infection and CD4 count has been established to be a standard laboratory marker of disease progression in HIV^{3, 24}. However in many resource limited countries, the cost of CD4 count are so high relative to reduced prices of antiretroviral drugs, that routine monitoring of therapy would often be more expensive than the supply of drugs themselves. Also unavailability of sophisticated laboratory

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equipment to measure CD4+ count precludes their use in large parts of the world. Previous studies had suggested that the total lymphocyte count (TLC) can be used to predict a low absolute CD4+ T cell.^{3, 27-30,}

According to WHO recommendation, when CD4 testing is unavailable, then patient can be started on HAART therapy, if patient has

- WHO stage IV disease irrespective of total lymphocyte count.
- WHO stage II or III disease with total lymphocyte count 1200 cells/mm³.

Treatment is also recommended for patients with advanced WHO stage II disease including recurrent or persistent oral thrush and recurrent invasive bacterial infections irrespective of CD4 count or TLC.

We undertook to look at the correlation between the CD4 count and TLC in HIV patients with advanced disease. CD4 counts of 200 or less were correlated with total lymphocyte count of 1200 or less.

It was also noted that patients had a mean CD4 count of 175 cells/mm³ and patients had a mean TLC of 1338 cells/mm³. These observations were comparable with other study groups.

On calculating linear correlation between CD4 count of <200 cells/mm³ and TLC of <1200, there was high statistical significance with sensitivity of 91%, specificity of 53% and positive predictive value of 70%.

The scatter diagram shows that as the CD4 count level increases the TLC level also increases and there was a significant correlation between CD4 and TLC.

The values of our study were correlated with other national and international studies

Place	NO. of pts.	Aim	Sensitivity	Specificity	TLC for CD4 <200 cells/mm ³	Results
John Hopkins University	1451	Correlation TLC & Hb% to predict CD4 <200 before initiation of HAART	78%	37.3%	<1200	TLC <1200 cells/mm ³ significantly predict CD4 count <200
			70.7%	81.8%	<1200	TLCC <1200 cells/mm ³ significantly predict CD4 count <200
YRG Centre for AIDS research and education Chennai, India	650	To evaluate the correlation of TLC to CD4 count	73%	50%	<1400	Correlated with CD4 <200 cell/mm ³
			70%	86%	TLC <1700/ CD4 <350	Significant correlation b/w TLC <1700 and CD4 <350 cells/mm ³

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YMCH, Mangalore	50	To correlate b/w CD4 count & TLC	91%	53%	TLC of 1200 or less correlate with CD4 count 200	Significant correlation b/w CD4 <200 & TLC 1200
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Apart from the studies mentioned above, R Wood, F Post and G Maartene, (Cape Town, South Africa).³⁰ also studied CD4 and total lymphocyte counts as predictors of HIV disease progression and concluded that for each clinical stage, a significant difference in progression to AIDS and mortality was predicted by TLC above or below 1250 cells/mm³. Survival and progression to AIDS occurred at similar rates in patients with TLC 1250 cells/mm³ or CD4 count of 200 cells/mm³.

Another study done by Beck EJ et al³², at Academic Department of Public Health, St Mary's Hospital Medical School, London, UK on 1534 paired Total Lymphocyte count and CD4 count, a significant correlation did exist and the high correlation between total and CD4 lymphocyte counts, especially for patients with symptomatic HIV disease, demonstrated the suitability of the use of TLC in the absence of CD4 counts. Given the considerably lower prices of TLCs compared with T- cell subset analysis, this is particularly relevant for developing countries.

To summarize, a total of 15, 102 patients enrolled in 15 different studies were followed up to determine the ability of the total lymphocyte count to predict the CD4 cell count and HIV disease stage³³. Eleven of these studies (which induced a total of 11, 713 patients) contained data that, overall, indicated support for the predictive ability of the total lymphocyte count, whereas four had concluded that TLC was not a reliable predictor of the CD4 cell count³³.

Studies done in John Hopkins University Bloomberg School of Public Health analyzed stated that a TLC decline of greater than 10% per year and Hemoglobin decline of greater than 22% per year was noted in over 77% of study participants who developed AIDS^{34, 20}

The pattern of CD4+ counts over time 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 count.²⁰

As the CD4 count is affected by the time of the day (lower in the morning), in acute illness, refrigeration of blood sample (decrease CD4+ counts) or with rough handling or contamination of blood sample, serial recording of TLC and hemoglobin can give an equally stable reflection of progression of disease and development of AIDS in HIV positive patients.³³

It becomes more feasible especially in developing countries as a CD4 count costs around \$ 30 US while TLC costs around 0.80 US \$³⁵, monitoring the patient with TLC will have an enormous cost benefit in patients with limited resources.

Limitations of this study necessitate further investigations. As this was an observational study of subjects in Mangalore, more assessment of TLC using data from the target countries are needed. Conditions specific to resource limited settings, such as the higher prevalence of leukocytosis due to inter current infections, may influence the interpretability of changes in TLC. Further, as has been shown with CD4 count, TLC values as well as the dynamics of the measure may vary across different ethnicities. Region-specific validation of CD4 and TLC changes on HAART are needed. Also, TLC measured by complete blood count may not be possible in very low income

countries or remote regions. Therefore, the evaluation of TLC measured by light microscopy and manual cell counting may be beneficial.

CONCLUSION:

- In this study we conclude that most of the clinical observations were in accordance with the other studies conducted earlier. The study showed male preponderance with heterosexual mode of transmission being the commonest mode of transmission. Fever, weight loss and diarrhea continue to be the presenting symptoms. Tuberculosis was the most common opportunistic infection. Among various neurological manifestations, tubercular meningitis was the commonest and unlike in other studies, there was absence of cryptococcal meningitis and toxoplasmosis in our study.
- Thus HIV infection can present with varied manifestations depending on geographic, socio-economic and cultural environment and thus needs a high index of suspicion for early detection of case and management.
- Our study shows a definite correlation between TLC and CD4 count in HIV positive patients. CD4 counts of less than 200 cells/mm³ showed a statistically significant correlation with TLC of less than 1200 cells/mm³
- TLC can be substituted for the CD4 count when the latter is unavailable and HIV related symptoms exist.
- TLC could be used as a low cost tool and as a surrogate marker for monitoring HIV disease and its progression.
- These results could be very useful for regions with scarce health care resources as an alternative way of identifying individuals who should receive HAART therapy for HIV infection. We believe further research in appropriate population is warranted.
- For the people who may not be able to afford the treatment and may get free supply of antiretroviral medicine, TLC can serve as a cost effective, affordable index to start HAART treatment and also to monitor HAART treatment.

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Date of Submission: 16/12/2013.
Date of Peer Review: 17/12/2013.
Date of Acceptance: 24/12/2013.
Date of Publishing: 26/12/2013.