



RESEARCH ARTICLE

TO CORRELATE QUANTITATIVE C-REACTIVE PROTEIN WITH CD4 COUNT IN PATIENTS OF HIV ON ART

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ABSTRACT

Introduction : The acquired immunodeficiency syndrome (AIDS), a disorder in which the immune system gradually fails and life-threatening opportunistic infections and malignancies proliferate, is brought on by the human immunodeficiency virus (HIV), a lentivirus (a member of the retrovirus family). Naturally C-Reactive Protein being an acute phase reactant should increase in patients with HIV disease progression if it is associated with microbial translocation and immune activation as hypothesized in studies. Many studies reported that there is a significant association of immune activation as measured by quantitative CRP levels with HIV disease progression. This study was designed to find the association between quantitative CRP and CD4 count in patients of HIV. **Method:** We retrieved and analyzed the data of 100 patients of HIV on ART between June 2020 to December 2021 at Department of General Medicine and Outpatient Department or ART Centre, RNT Medical College and assigned group of Hospitals, Udaipur. **Results :** Majority of the subjects are on TLE (82%) regimen, followed by TLD (17%) and ZLN (1%). Majority patients had opportunistic infections and predominant was oral candidiasis (24%) followed by LRTI(17%), diarrhea (16%), tubercular meningitis(10%) and pulmonary TB(8%). 22% patients didn't have any opportunistic infections. Among opportunistic infection as the severity of the infection increases, mean CRP levels among them increased, this shows positive correlation of mean CRP with severity of the infection statistically significant with p value = 0.000. Among opportunistic infection as the severity of the infection increases, mean CD4 levels among them decreased, this shows negative correlation of mean CD4 with severity of the infection, statistically significant with p value = 0.000. As the CD4 levels decrease, there is increase in CRP levels, so there is significant negative correlation between mean CD4 and mean CRP among subjects with different above labelled opportunistic infection. There is mean CRP of 22.52 mg/dl & Mean CD4 of 229.84 cells/cumm. As they both are negatively correlated and hence statistically significant with Pearson Correlation, r value = -0.770 p value = 0.000. **Conclusion:** Elevation of CRP is associated with a low count of CD4 in HIV diagnosed patients. Thus, serum CRP levels can be used as marker of immunosuppression and type of opportunistic infection in resource-limited areas where CD4 count availability is difficult.

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INTRODUCTION

Acquired immunodeficiency syndrome (AIDS) was first recognized in the United States, when the Centres for Disease Control and Prevention (CDC) reported the unexplained occurrence of Pneumocystis jirovecii pneumonia in five previously healthy homosexual men in Los Angeles and of Kaposi's sarcoma with or without pneumocystis jirovecii pneumonia and other opportunistic infections in 26 previously healthy homosexual men in New York, San Francisco, and Los Angeles in the summer of 1981, the condition was first identified (1). The acquired immunodeficiency syndrome (AIDS), a disorder in which the immune system gradually fails and life-threatening opportunistic infections and malignancies proliferate,

is brought on by the human immunodeficiency virus (HIV), a lentivirus (a member of the retrovirus family)(2, 3). Globally, an estimated 1.8 million new cases of HIV infection were reported in 2016, with 160 000 of those cases affecting children under the age of 15. A third of these infections affected persons between the ages of 15 and 24. The number of AIDS-related deaths worldwide reached 1.0 million in 2016 (including 120 000 children under the age of 15), a 48% drop from 2005 and one that is correlated with an explosive increase in antiretroviral medication access. An estimated 35 million people have passed away from an AIDS-related ailment since the pandemic's start. (1) The first case of HIV was discovered in Chennai, Tamil Nadu, in 1986, while the first instance of AIDS was discovered in Mumbai, Maharashtra, in 1987. In India, there are around 5.206

million HIV-positive individuals as of 2006. AIDS affects 21.5% of women and 78.5% of men in a 3:1 ratio, although more and more women are getting the disease. (4) With the introduction of highly active antiretroviral therapy (HAART) over the past two decades, HIV patients' life expectancy has significantly increased. As a result, attention is now being paid to treating long-term effects of HIV infection and enhancing the lives of HIV patients, particularly in wealthy countries. On the other hand, developing countries' fragile economies are being severely burdened by the ever-rising incidence of HIV infection, necessitating the need for more affordable alternatives to traditional, more expensive measures like CD4 count and HIV RNA load as well as for simplification of HIV treatment protocols. (5) CRP was first identified by Tillett and Francis in 1930 as a substance in the serum of patients with acute inflammation that reacted with the C-polysaccharide of pneumococcus (hence the name). (6) Later, it was found to be an acute phase reactant with a pentameric structure that remains stable for a sufficiently long time, allowing measurements of 1000s of stored serum samples. (7) Most CRP is produced from liver apart from vascular endothelium in response to interleukin-6 produced from macrophages and adipocytes. (8, 9) Normally its serum concentration is less than 6mg/L, but during inflammation its level may increase 10, 000-folds. Increase in CRP level can be detected as early as 5-10 hours after tissue damage. Immune activation has been demonstrated to be a significant contributor to HIV disease progression in multiple studies. It was observed that this immune activation was associated with increased levels of bacterial components in blood, which was hypothesized to be due to increased microbial translocation from the gastrointestinal tract of patients and this microbial translocation was hypothesized to contribute for HIV disease progression. Naturally CRP being an acute phase reactant should increase in patients with HIV disease progression if it is associated with microbial translocation and immune activation as hypothesized in studies. (5) Many studies reported that there is a significant association of immune activation as measured by quantitative CRP levels with HIV disease progression. This study was designed to find the association between quantitative CRP and CD4 count in patients of HIV.

METHODS

The study was a Cross Sectional Observational Study conducted at Department of General Medicine and Outpatient Department or ART Centre, RNT Medical College and assigned group of Hospitals, Udaipur from June 2020 to December 2021 after obtaining approval from Institution Ethics Committee. All patients of HIV on ART in various wards of Department of General Medicine or attending Outpatient Department or ART Centre for regular follow up, RNT Medical College and assigned group of Hospitals, Udaipur were enrolled in the study after considering the inclusion and exclusion criteria. Informed consent was taken from study subjects and detailed history regarding age, sex, occupation, mode of transmission and status of other family members were obtained. We excluded patients below age of 18 years, patients who were known case of rheumatoid arthritis, connective tissue disorders and cancers & patients with pre-existing liver, kidney and heart disease. Consecutive Sampling was used. The following investigation were done on study subjects

- CBC Hb, MCV, TLC, DLC, Platelet Count, RBC, WBC, Platelets.
- LFT AND RFT, SGOT, SGPT, ALP, Total Bilirubin, Direct and Indirect bilirubin, Total Protein, Albumin, Urea, Creatinine.
- CD4 COUNT done by Flow cytometry (FC) method at ART centre of RNT medical college.
- Quantitative CRP done by capillary tube method in central laboratory.

Data Assessment: The results were tabulated and subjected to statistical analysis. Statistical tests used included mean, standard deviation, ANOVA (analysis of variance), chi-square test. The data was entered in Microsoft office 2013 Excel worksheet and statistical analysis was done using SPSS version 12. Descriptive statistics were applied; p value less than 0.05 was considered statistically significant.

RESULTS

In this study 100 study subjects were enrolled for the study after applying inclusion and exclusion criteria during the period from June 2020 to Dec 2021. Majority of the subjects are on TLE(82%) regimen, followed by TLD(17%) and ZLN(1%).

Table I. Number of patients on ART regimen in the study

ART regimen	Number	Percentage
TLE	82	82.0
TLD	17	17.0
ZLN	1	1.0
Total	100	100.0

Majority patients had opportunistic infections and predominant was oral candidiasis (24%) followed by LRTI (17%), diarrhoea (16%), tubercular meningitis (10%) and pulmonary TB (8%). 22% patients didn't have any opportunistic infections.

Table II. Number of patients with opportunistic infection in the study subjects

Opportunistic infections	Number	Percentage
None	22	22.0
Diarrhoea	16	16.0
LRTI	17	17.0
Oral candidiasis	24	24.0
Pulmonary TB	8	8.0
Tubercular meningitis	10	10.0
Cryptococcal meningitis	2	2.0
Toxoplasmosis	1	1.0

Among opportunistic infection as the severity of the infection increases, mean CRP levels among them increased, this shows positive correlation of mean CRP with severity of the infection statistically significant with p value = 0.000. Among opportunistic infection as the severity of the infection increases, mean CD4 levels among them decreased, this shows negative correlation of mean CD4 with severity of the infection, statistically significant with p value = 0.000. As the CD4 levels decrease, there is increase in CRP levels, so there is significant negative correlation between mean CD4 and mean CRP among subjects with different below labelled opportunistic infection. There is mean CRP of 22.52 mg/dl & Mean CD4 of 229.84 cells/cumm. As they both are negatively correlated and hence statistically significant with Pearson Correlation, r value – 0.770 p value = 0.000.

DISCUSSION

In my study, which included 100 patients of HIV infection on ART in various wards of Department of General Medicine or Outpatient Department or ART Centre for regular follow up, RNT Medical College and assigned group of Hospitals, Udaipur. Majority of the patients belonged to age 31 to 40 years (51%), which is comparable with Gahlot et al⁽¹⁰⁾, Chaudhary et al⁽¹¹⁾, Sunitha et al⁽¹²⁾, Rajshekar et al⁽¹³⁾ studies. In my study, male predominantly affected, which is 63.0%, which is comparable with Chaudary et al⁽¹¹⁾, Sunitha et al⁽¹²⁾, Rajshekar et al⁽¹³⁾ studies.

In my study, among occupation, housewives are affected most, which is 34%, followed by drivers an coolie workers which is 21% each, that is comparable with Kumawat S et al⁽¹⁴⁾, Singh et al⁽¹⁵⁾ studies. In my study, majority of the patients are married, that is 97%, which is comparable with Chaudary et al⁽¹¹⁾, Sunitha et al⁽¹²⁾ studies. In my study, the mode of transmission was Not known in 71%, heterosexual in 29%. which is comparable with Kumawat S et al⁽¹⁴⁾, Singh et al⁽¹⁵⁾ studies. In my study, majority of the subjects are on TLE (77.8%) regimen, followed by TLD (18.8%) and ZLN(3.5%), which is comparable with Gahlot et al⁽¹⁰⁾, Chaudary et al⁽¹¹⁾

Table III. Mean CRP among patients with opportunistic infection in the study

	N	Mean	S.D.	S.E.	95% Confidence Interval for Mean	
					Lower Bound	Upper Bound
None	22	8.68	3.014	0.643	7.35	10.02
Diarrhoea	16	12.56	6.000	1.500	9.37	15.76
LRTI	17	19.18	7.772	1.885	15.18	23.17
Oral candidiasis	24	26.42	7.046	1.438	23.44	29.39
Pulmonary TB	8	30.88	14.257	5.041	18.96	42.79
Tubercular meningitis	10	45.20	8.942	2.828	38.80	51.60
Cryptococcal meningitis	2	59.00	1.414	1.000	46.29	71.71
Toxoplasmosis	1	83.00	--	--	--	--
Total	100	22.52	15.361	1.536	19.47	25.57

Anova value (F) 48.461, p value = 0.000

Table VI. Mean CD4 count among patients with opportunistic infection in the study

	N	Mean	S.D.	S.E.	95% Confidence Interval for Mean	
					Lower Bound	Upper Bound
None	22	406.86	98.235	20.944	363.31	450.42
Diarrhoea	16	296.19	91.436	22.859	247.46	344.91
LRTI	17	219.00	114.075	27.667	160.35	277.65
Oral candidiasis	24	125.25	26.612	5.432	114.01	136.49
Pulmonary TB	8	174.88	154.402	54.590	45.79	303.96
Tubercular meningitis	10	98.30	27.504	8.697	78.63	117.97
Cryptococcal meningitis	2	76.00	18.385	13.000	-89.18	241.18
Toxoplasmosis	1	31.00
Total	100	229.84	143.374	14.337	201.39	258.29

Anova value (F) 23.668, p value = 0.000

Table V. Correlation of mean CRP and mean CD4 in patients with opportunistic infection in the study subjects

Opportunistic infections	Mean CRP	Mean CD4 count
None	8.68	406.86
Diarrhoea	12.56	296.19
LRTI	19.18	219.00
Oral candidiasis	26.42	125.25
Pulmonary TB	30.88	174.88
Tubercular meningitis	45.20	98.30
Cryptococcal meningitis	59.00	76.00
Toxoplasmosis	83.00	31.00

Table VI. Mean CRP and mean CD4 in patients with opportunistic infection in the study subjects

	Mean	SD	N
CD4	229.84	142.65	100
CRP	22.52	15.28	100

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