

# CORRELATION OF QUANTITATIVE C - REACTIVE PROTEIN WITH CD4 COUNT IN PATIENTS OF HIV ON ART

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## Abstract

**Introduction:** Infections in people living with HIV reflect the immune suppression of the host. Hence, CRP can be used as a marker of degree of immune suppression. CRP is produced as a result of the opportunistic infection; a decreased level of CRP is thus an indicator of good treatment response to the underlying infection. Present study is an effort to evaluate correlation as well as association between CD4 count and CRP levels in HIV/AIDS.

**Methodology:** The present study was a cross sectional hospital based study for a period of twelve months from 1<sup>st</sup> Nov. 2015 to 31<sup>st</sup> Oct. 2016 at ART center P.B.M. Hospital, Bikaner. Out of 100 HIV + patients on ART, 50 were symptomatic and included in study group and remaining 50 were asymptomatic and taken as control.

**Results:** Maximum no of participants in both groups were between age group of 31-40 years; were male; were from Bikaner; were married; were of low socioeconomic status; and had history of heterosexual contacts. Mean duration since ART started was 2-5 years in 50% cases and 52% of controls respectively. In our study 38% of the study group patients had CRP>20 mg/l whereas 88% of the control subjects had CRP of <6mg/l. 46% of the study subjects had CD4 count less than 200 as compared to just 4% in the control group. CRP level was significantly higher in study group and CD4 count was higher in control group. Highest CRP level were found for TB followed by oral candidiasis, LRTI and diarrhea.

**Conclusion:** From the study conducted it can be concluded that hsCRP is an excellent predictor of OI risk in HIV patients. So the additional cost of doing hsCRP assay in all newly detected patients would be justifiable.

**Key Words:** 1. Quantitative CRP 2. Opportunistic infection 3. CD4 count 4. ART (antiretroviral therapy)

## INTRODUCTION

Opportunistic infection accounts for the majority of death in untreated patients with HIV. CRP levels increase with infection and there exists a negative correlation between CRP and CD4 count<sup>1</sup>. Infections in people living with HIV reflect the immune suppression of the host. Hence, CRP can be used as a marker of degree of immune suppression. CRP is produced as a result of the opportunistic infection; a decreased level of CRP is thus an indicator of good treatment response to the underlying infection. 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.<sup>2,3</sup>

Very few studies have been performed in India on this issue; therefore present study is an effort to evaluate correlation as well as association between CD4 count and CRP levels in HIV/AIDS.

## Aims And Objective

1. To establish a relation between CD 4 count and CRP levels.
2. To obtain an association between CRP levels and symptoms of opportunistic infection.

## METHOD AND MATERIAL

The present study was a cross sectional hospital based study for a period of twelve months from 1<sup>st</sup> Nov. 2015 to 31<sup>st</sup> Oct. 2016 at ART center P.B.M. Hospital, Bikaner. 100 HIV+ patients on ART were included in the study. Out of 100 patients, 50 were symptomatic and included in study group and remaining 50 were asymptomatic and taken as controls.

## Inclusion criteria

1. Age more than 18 years
2. Patients sero positive for HIV-antibodies
3. Patients on ART at least 6 months
4. Ready to give consent.

## Exclusion criteria

1. Patients below age of 18 years.
2. Patients who were known case of rheumatoid arthritis, connective tissue disorders and cancers.
3. Patients with pre existing liver, kidney and heart disease.

## RESULTS

Maximum number of study participants in age group of 31-40 years in both study (50%) and control (42%) group. Males were higher in study (76%) as well as control (64%) group than females. Maximum number of study subjects was from Bikaner with 74% of subjects in cases and 64% in controls. Among the subjects mostly belonged to lower socioeconomic status. Most of the subjects in study (92%) as well as control (94%) were married. Mean duration since first diagnosed was higher in control group (4.39 years) than study group (4.05 years) but the difference was not statistically significant. Duration since ART with most of the subjects in both group is 2-5 years followed by <2year and > 5 years. Maximum study subjects had route of heterosexual contact (86%) followed by others (8%) and homosexual (6%) whereas the controls had route of contact maximum with heterosexual (94%) followed by homosexual (4%) and others (2%). There was significant statistical difference between routes of contact.

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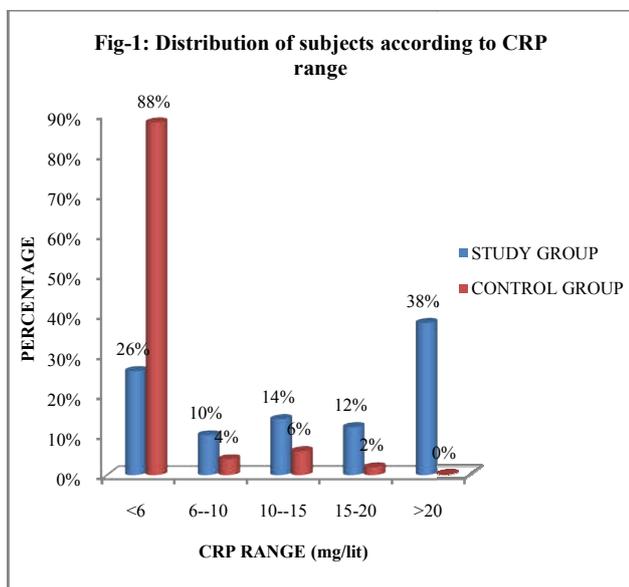
Table 1a shows that 37 (74%) patients in study group had CRP levels >6 mg/lit (normal level <6 mg/lit). Out of 37, 19 subjects (38% of total) had CRP level >20 mg/lit. While in control group, 44 subjects (88%) had CRP level <6 mg/lit. Only 6 (12%) subjects of control group had CRP level >6mg/lit.

None of control subjects had CRP level >20 mg/lit.

Therefore it was observed that study group patients who had Opportunistic infections had higher levels of CRP as compared to control group and this difference was statistically significant (p=0.0001).

**Table 1a** Distribution of subjects according to CRP Range

Range of CRP (mg/lit)	Group		P value
	STUDY	CONTROL	
<6	13 (26%)	44 (88%)	$\chi^2=35.84$ 0.0001 (Significant)
6-10	5 (10%)	2 (4%)	
10-15	7 (14%)	3 (6%)	
15-20	6 (12%)	1 (2%)	
>20	19 (38%)	0 (0%)	
Total	50 (100%)	50 (100%)	



Also the mean CRP level in study group was significantly higher as compared to control group (p=0.0001). (Table-1b)

**Table 1b** Distribution of subjects according to CRP level

Level of CRP (mg/lit)	Group		Z test
	STUDY	CONTROL	
CRP levels	25.22 ± 3.41	5.39 ± 3.64	Z=23.71 P=0.0001 (Significant)

Table 2a shows comparative description of CD4 count range between 2 groups. 8% of study subjects as compared to 44% patients in control group were having CD4 count >500 /cumm. 46% of patients in study group were having CD4 count in the range of 200-500 cells/cumm whereas among controls this proportion was higher (52%). Around 30% cases in study group had CD4 count in range of 100-200 cells/cumm while only 4% cases in control group had CD4 count in this range. None of controls were having CD4 count <100 cells/cumm whereas among study group, 16% cases were having CD4 count <100 cells/cumm. Therefore it was observed that study group patients who had Opportunistic infections had lower ranges of CD4 counts as compared to

control group and this difference was statistically significant (p=0.0001).

Also the mean CD4 count in study group was significantly lower as compared to control group (p=0.0001). (Table 2b)

**Table 2a** Distribution of subjects according to CD4 count Range

Range of CD 4 (cells per cumm)	Group		P value
	STUDY	CONTROL	
<50	2 (4%)	0 (0%)	$\chi^2=29.98$ 0.0001 (Significant)
50-100	6 (12%)	0 (0%)	
100-200	15 (30%)	2 (4%)	
200-500	23 (46%)	26 (52%)	
>500	4 (8%)	22 (44%)	
Total	50 (100%)	50 (100%)	

**Table 2b** Distribution of subjects according to CD4 Count

CD 4 count (cells per cumm)	Group		Z test
	STUDY	CONTROL	
	249.96 ± 171.25	424.74 ± 166.51	Z= 32.453 P=0.0001 (Significant)

Table 3 shows that The CRP levels were increased till the CD4 count 150 cu mm. CRP level were minimum in patients with CD4 count between 151-200. The variation was statistically significant.

**Table 3** Changes in CRP levels among Cases as per CD4 count

CD4 count	CRP Level	
	Mean	SD
<50	8.4	.01
51-100	37.5	18.19
101-150	80.94	48.51
151-200	12.05	9.91
201-500	19.19	18.02
>500	35.06	30.57

F=8.52, P=0.0001

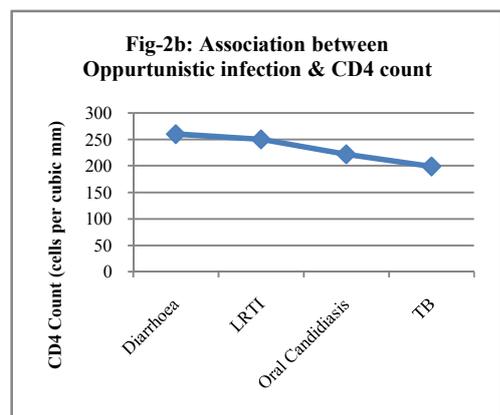
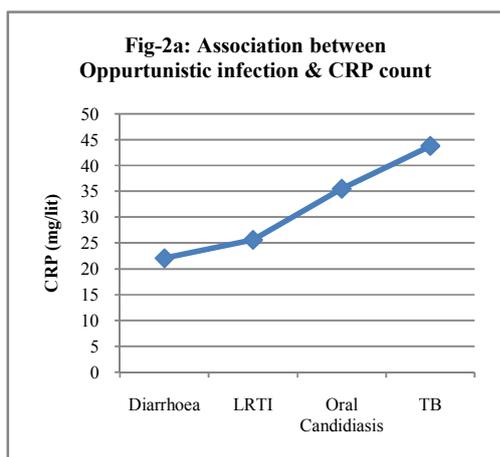
Table 4 shows that patients with HIV+TB had the highest CRP levels and lowest CD4 count followed by oral candidiasis patients who had 2<sup>nd</sup> highest CRP levels and 2<sup>nd</sup> lowest CD4 count.

The association between CRP levels and type of opportunistic infection shows highest CRP level for TB followed by Oral candidiasis, LRTI and diarrhoea. This difference in CRP levels with opportunistic infection was found to be statistically significant.

Also, CD 4 count was minimum for TB and maximum for diarrhoea in both the groups. There was statistically highly significant difference between each symptom and CD 4 count.

**Table 4** Association between CRP levels, CD4 count and type of opportunistic infection.

Symptoms of opportunistic infection	CRP levels	CD4 count
Diarrhoea	22.06 ± 4.72	260 ± 112.2
LRTI	25.60 ± 7.3	250 ± 82.3
Oral Candidiasis	35.47 ± 19.01	222 ± 101.2
TB	43.75 ± 20.21	199 ± 112.3
ANOVA, p value	0.0001	0.041



The CRP levels and CD4 count were negatively correlated in study group and this was observed to be statistically significant (p=0.04) whereas in control group, the CRP levels and CD4 counts were found to be very weakly positively correlated and this correlation was observed to be statistically insignificant.(Table5)

**Table 5** Correlation of CRP and CD 4 count in both the groups.

	Pearson Correlation (r)	P value
Study group (CRP with CD4)	1: -0.291	0.040 (Significant)
Control group (CRP with CD4)	1: 0.089	0.539 (Not Significant)

**DISCUSSION**

Maximum number of study participants in age group of 31-40 years in both study (50%) and control (42%) group and this matches with National AIDS Control Organization Technical Report<sup>4</sup> data, 2015 estimation that adult 15+ population contributed to almost half of PLHIVs.

Males were higher in study (76%) as well as control (64%) group than females as this disease affects males more because of heterosexual nature. Similar proportion is reported by NACO<sup>4</sup>, as females in PLHIV group being 40.5%.

Among the subjects mostly belonged to lower socioeconomic status followed by Medium and High socioeconomic status, this may be contributed to higher education status and more

awareness among medium and high socio economic class patients.

The statistical association of age, gender, place of residence, SES, Marital status and mean duration since first diagnosed and since ART in both the groups was found to be statistically not significant.

Highest CRP level for TB followed by Oral candidiasis, LRTI and diarrhoea. Sharma SK *et al* (2011)<sup>5</sup> in their study of studying incidence of immune reconstitution inflammatory syndrome (IRIS) among HIV patients observed that the commonest forms of IRIS are associated with mycobacterial infections, fungi and herpes viruses. Kala Yadhav ML *et al* (2012)<sup>6</sup> conducted a study at Victoria Hospital Bangalore, where a total of 171 HIV patients were enrolled to study type of opportunistic infections (OI), CRP level and treatment history of the underlying OI. Of the 86 tuberculosis patients, 23 had no history of treatment and CRP was found to be 41.2 mg/L. Ugwu MC *et al* (2016)<sup>7</sup> also observed that CRP levels were significantly higher in Cases as compared to controls and CD4 count was significantly lower among cases. The CRP levels and CD4 count were negatively correlated in study group and this was observed to be statistically significant (p=0.04). Similar findings were observed by Vishwanath A *et al* (2016)<sup>8</sup>. In present study in control group, the CRP levels and CD4 counts were found to be very weakly positively correlated and this correlation was observed to be statistically insignificant. The CRP levels and ART duration were negatively correlated in study group and this was observed to be statistically insignificant (p=0.172) whereas in control group, the CRP levels and CD4 counts were found to be very weakly positively correlated and this correlation was also observed to be statistically insignificant (p=0.665).

**CONCLUSION**

Quantitative CRP is a reliable marker of disease progression and a cheaper alternative for routine disease monitoring and predicting HIV-related outcomes, especially in a resource-poor setting.

Our study also suggests an important role of quantitative CRP in diagnosis of OIs. When HIV patient is affected by OIs its quantitative CRP levels also increases. Different OIs have different levels of CRP. As severity of infection increases CRP level also increases in proportion. In our study patients with pulmonary tuberculosis have highest levels of CRP and patients with diarrhea and LRTI have lowest.

Studies with larger number of patients are required to exactly correlate quantitative CRP with CD4 count. Even we can reach a formula which will approximately detect the CD4 count and possibly type of OI by quantitative CRP.

Further studies are required to understand the changes in quantitative CRP levels after HAART therapy.

From the studies conducted till date it can be safely concluded that quantitative CRP is an excellent predictor of OI risk in HIV patients. The importance of evaluating, preventing, and managing CVD in patients with HIV is recognized in guidelines for the use of antiretroviral agents in HIV-infected adults. Because quantitative CRP is cheap to measure and easily available, it may become a clinically useful tool to monitor OI risk in HIV-positive patients.

Therefore the additional cost of doing a quantitative CRP assay in all newly detected patients would be justifiable.

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