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Original Article

Correlation between High-density Lipoprotein Cholesterol Level and CD4 Cell Count in HIV Patients on NNRTI-based ART Regimen at Tertiary Care Hospital in Mysuru

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Abstract

Introduction: India accounts for roughly half of Asia's HIV prevalence. ART can prolong quality of life in HIV infected patients. The current follow up pattern in India is on the basis of CD4 counts which are done in higher ART centers once in 6 monthsThe lipid derangement is very well known to happen in HIV patients patients on ART. In this study we tried to evaluate changes in lipid profile with CD4 counts of patients on ART.Since lipid profile can be done even in peripheral set up and it is economical, it will help in the management of HIV patients in peripheral centres

Material and Methods: 102 HIV patients visited ARTC at KR Hospital Mysore (starting from Dec 2013 to Dec 2014) age group between 20-50 yrs on NNRTI based ART for a minimum of 3 months are included in this study. For all the patients CD4 count leveland lipid profile is done.

Results: Out of 102 patients included in the study, majority were males [73%] and mean age group was 37.12 yrs. when CD4 count considered, majority of females [86%] had CD4 count >200. This may indicate good drug compliance among females when considered to males.Correlation analysis shows that there is significant correlation between CD4 count and HDL while other parameters of lipid profile show no significant correlation. This concludes high HDL value in a patient on NNRT can indicates high CD4 count and a good immunity.

Conclusion: This study confirms that, the HDLcholeterol has significant impact in predicting the level of CD4 cell counts in treating with NNRTI ART regimen and we found positive correlation between both the parameters.So HDL cholesterol Which is more economical test, even can be done in peripheral centres to assess the over all general condition of the patients on ART.

Key words: HIV ,NNRTI, HDL cholesterol, CD4 count, lipoproteins

INTRODUCTION

The first cases of HIV infection in India were documented in 1986 among female sex workers (FSWs) in Chennai, Tamil Nadu. Subsequently, cases of HIV infection have been reported from every state. The HIV epidemic in India has followed the "type 4 pattern," where new infections occur first among the most vulnerable populations (such as FSW and injecting drug users [IDU]), then spread to "bridge" populations (clients of sex workers and sexual partners of drug users) and then finally enter the general population.[1]

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A critical review of the HIV epidemic in India reveals the following trends:

- Young adults (15-49 years) account for 89% of the burden of HIV infection.
- The male-to-female ratio is 3:2.
- The states of Andhra Pradesh, Maharashtra, Karnataka, West Bengal, Tamil Nadu, Gujarat, and

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Uttar Pradesh together account for 80% of the burden in India. The prevalence is <1% in the Northeastern states of Nagaland and Manipur.

- India has a "concentrated epidemic," the prevalence being significantly higher among various high-risk groups (MSM, IDU, FSW, and STD clinic attendees) than among antenatal clinic (ANC) attendees.
- There is considerable variability in the spread of HIV infection in the country. At the district level, 87 districts had HIV prevalence <1% among ANC attendees and 47 had <5% prevalence among FSW in 2007. Several of these districts are in moderate and low-prevalence states such as Bihar, Chhattisgarh, West Bengal, and Gujarat.
- The predominant mode of transmission is heterosexual exposure, while it is injecting drug use in Northeastern states.
- HIV prevalence has been stable from 2002 to 2007.
- HIV prevalence among women attending ANC has declined from 2000 to 2007, indicating a decrease in the incidence of new infections.[1]
- ART can prolong the quality of life in HIV-infected patients. However, this needs a regular follow-up.
- Moreover, current follow-up pattern is on the basis of CD4 counts which are done in higher ART centers once in 6 months.
- Lipid derangements in HIV are a well-known fact. In this study, we tried to evaluate changes of CD4 count and lipid profile in HIV patients on first-line ART regimen to find out any possible correlation between these two parameters.
- If we can assess CD4 count with other parameters which can be done even in peripheral setup, then it will be easy to assess the general condition of the patient and will help to manage the HIV patients in peripheral centers. It will also help the physicians to assess the level of immunity in HIV-infected patients without a regular follow-up in ART centers.

Monitoring CD4+T Cell Counts

The CD4+T cell count is the laboratory test generally accepted as the best indicator of the immediate state of immunologic competence of the patient with HIV infection.

This measurement, which can be made directly or calculated as the product of the percentage of CD4+T cells (determined by flow cytometry) and the total lymphocyte count (determined by the white blood cell count (WBC) multiplied by the lymphocyte differential percent), has been shown to correlate very well with the level of immunologic competence.

Patients with CD4+T cell counts <200/dL are at high risk of disease from *Pneumocystis jirovecii*, while patients with CD4+T cell counts <50/dL are at high risk of disease from CMV, mycobacteria of the *Mycobacterium avium* complex (MAC), and/or *Toxoplasma gondii*.

Patients with HIV infection should have CD4+T cell measurements performed at the time of diagnosis and every 3-6 months thereafter. More frequent measurements should be made if a declining trend is noted.

According to the U.S. Department of Health and Human Services Guidelines, a CD4+T cell count <500/dL is an indication for initiating cART, and a decline in CD4+T cell count of >25% is an indication for considering a change in therapy. Once the CD4+T cell count is <200/dL, patients should be placed on a regimen for *P. jiroveci* prophylaxis, and once the count is <50/dL, primary prophylaxis for MAC infection is indicated.

As with any laboratory measurement, one may wish to obtain two determinations before any significant changes in patient management based on CD4+T cell count alone. There are a handful of clinical situations, in which the CD4+T cell count may be misleading. Patients with HTLV-1/HIV coinfection may have elevated CD4+T cell counts that do not accurately reflect their degree of immune competence. In patients with hypersplenism or those who have undergone splenectomy and in patients receiving medications that suppress the bone marrow such as IFN-, the CD4+T cell percentage may be a more reliable indication of immune function than the CD4+T cell count. A CD4+T cell percent of 15 is comparable to a CD4+T cell count of 200/dL.[2]

Principles of Antiretroviral Therapy

A continuous high level of replication of HIV takes place in the body right from the early stages of infection. At least one billion viral particles are produced and destroyed each day. The antiretroviral drugs act on various stages of replication of HIV in the body and interrupt the process of viral replication. Theoretically, these drugs can act at the many steps in viral replication. Most commonly used drugs target the virus mainly by inhibiting the enzymes reverse transcriptase (RT) inhibitors and protease inhibitors.

Based on the scientific evidence, therapy guidelines have been developed by various international agencies such as the WHO, DHHS, BHIVA, and IAS. They define the optimum time, parameters, and drugs to initiate and sequence treatment.[3]

Recommended Choices of First-line Regimens

Principles for selecting the first-line regimen:

1. Choose 3TC (lamivudine) in all regimens
2. Choose one NRTI to combine with 3TC (AZT or d4T)
3. Choose one NNRTI (NVP or EFV).

Lipid Disorders in HIV Infection

The lipid disorders seen in individuals with HIV infection include elevated triglycerides (TG) and total cholesterol (TC), a decrease in high-density lipoprotein (HDL) cholesterol, and variable effects on low-density lipoprotein (LDL) cholesterol.[4] The exact mechanism is still not clear, and the cause could be multifactorial. The individual contributions of HIV infection, specific antiretroviral agents, host genetics, and changes in body composition all should be considered.

Effect of HIV Infection on Lipid Profile

Abnormalities of lipid metabolism in HIV-infected patients were described before the use of HAART.[5-7] Increased serum TG and reduced TC concentrations were observed in advanced HIV infection. Patients with advanced HIV infection or with AIDS have also had lower levels of HDL-C and LDL-C, increased TG level, and a predominance of small, dense LDL particles compared with HIV-negative individuals. In the early 1990s, a number of investigators described the lipid abnormalities associated with HIV infection. A consistent finding from these studies was that patients with advanced HIV infection or AIDS had high levels of circulating TG and low levels of HDL cholesterol.[7,8]

METHODOLOGY

Study design contains two populations, visiting ART center in Krishna Rajendra Hospital starting from December 2013 to December 2014.

1. HIV-infected patients on NNRTI with CD4 counts >200 males and females.
2. HIV patients on NNRTI with CD4 counts <200 males and females.

Method of Collection of Data (Including Sampling Procedures if Any)

In Karnataka state, 2.5 lakh HIV-positive patients are taking ART treatment.

Sample size - 102 HIV-seropositive patients on NNRTI will be studied.

Sampling Method - Purposive Sampling

Statistical methods are Pearson correlation analysis, linear regression, and multivariate regression model.

- It is an exploratory study, in which HIV patients on NNRTI will be evaluated by CD4 count, and their HDL cholesterol level will be checked by the automated chemical analyser.
- NNRTI includes zidovudine or stavudine, lamivudine, and nevirapine in this study.

HIV-infected patients both males and females age group between 20 years and 60 years started on NNRTI (zidovudine or stavudine, lamivudine, and nevirapine) based ART for a minimum of 3 months and who are taking these drugs regularly included in this study.

HIV-infected patients on other regimens of HAART, HIV-infected patients on irregular treatment, hypertensives, and pregnancy were excluded from the study.

RESULTS

In this study, mean age group of the patients included is 37.12. When observing the age distribution of the included patients, 39% of the population were in between 35 and 41 years of age.

In this study, patients further grouped into two. CD4 count <200 group had a mean age of 35.67 years (SD of 7.76) and CD4 count >200 group had a mean age of 38.64 years (SD of 7.19). This observation is consistent with other studies conducted in India and abroad (Table 1).

In the present study, 27 patients (27%) were female and 74 patients were male (73%). This is consistent with a study conducted by Enrique Bernal *et al.*, with male patients constituting 79%, Swiss HIV cohort study showed that male patients constituted 68%, and the study done by Indumati *et al.* showed that male patients constituted 60%. This indicates that most of the HIV patients taking ART treatment in ART centers are males (Table 2).

In this study, HIV patients on NNRT-based ART grouped into 2 categories with respect to CD4 count. CD4 count <200 had mean TC of 218.67 and CD4 count >200 had mean cholesterol of 185.36. Mean TC value is statistically same among patients with CD4 <200 and CD4 >200, $P = 0.37$ indicates that the mean value of TC among patients with CD4 <200 and CD4 >200 is same (Table 3).

In this study, HIV patients on NNRT-based ART grouped into 2 categories with respect to CD4 count. CD4 count <200 had mean TG of 248.08 and CD4 count >200 had mean TG of 213.31. Mean TG value is statistically same among patients with CD4 <200 and CD4 >200, $P = 0.34$

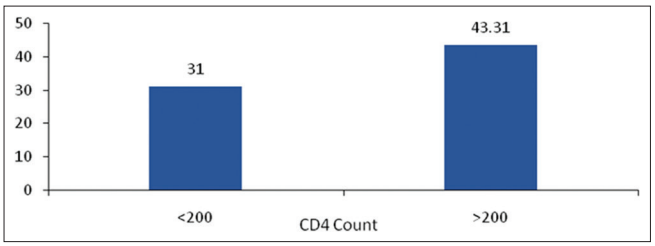
Table 1: Sex distribution and CD4 count

Sex	CD4 count	Number of patients (%)
Female	<200	4 (14)
	>200	24 (86)
Male	<200	20 (27)
	>200	54 (73)

indicates that the mean value of TG among patients with CD4 <200 and CD4 >200 is same (Table 4).

In this study, HIV patients on NNRT-based ART with CD4 count <200 had mean LDL 88.08 and CD4 count >200 had mean LDL 99.05. Mean LDL value is statistically same among patients with CD4 <200 and CD4 >200, $P = 0.07$ indicates that the mean value of LDL among patients with CD4 <200 and CD4 >200 is same (Table 5).

In this study, HIV patients on NNRT-based ART with CD4 count <200 had mean HDL 31 and CD4 count >200 had mean HDL 43.31. Mean HDL with CD4 <200 and CD4 >200 is statistically different. $P = 0.0$ indicates that mean is not same among the patients with CD4 <200 and CD4 >200 (Graph 1).



Graph 1: Mean high-density lipoprotein by CD4 count

DISCUSSION

Correlation analysis shows that there is a significant correlation between CD4 count and HDL while other parameters of lipid profile show no significant correlation at 5% significance level.

- TC has an insignificant impact on predicting CD4 count at 5% significance level.
- TG has an insignificant impact on predicting TG at 5% significance level.

HDL has significant impact in predicting the CD4 counts at 5% significance level. R-square is 25.5% and $P = <0.0001$ which indicates that impact of HDL on CD4 count is highly statistically significant.

LDL has an insignificant impact in predicting CD4 count at 5% significance level. $P = 0.21$ indicates that impact is statistically insignificant at 5% significance level.

Multiple regression model is developed to measure the impact of all the lipid profile variables in predicting CD4 counts. Impact of TC and HDL is statistically significant at 5% significance level.

Table 2: Mean TC and CD4 count

Total cholesterol	*n*	Minimum	Maximum	Mean±SD	Variance	*t*-value (*t*-test)	*P*-value
CD4 count	24	125	772	218.67±175.37	30754.63	0.92	0.37
<200	78	116	286	185.36±41.03	1683.46		
>200							

TC: Total cholesterol, SD: Standard deviation

Table 3: TG distribution

TG	*n*	Minimum	Maximum	Mean±SD	Variance	*t*-value (*t*-test)	*P*-value
CD4 count	24	81	588	248.08±160.67	25814.84	0.98	0.34
<200	78	71	645	213.31±121.07	14657.94		
>200							

TG: Triglycerides, SD: Standard deviation

Table 4: LDL Distribution

LDL	*n*	Minimum	Maximum	Mean±SD	Variance	*t*-value (*t*-test)	*P*-value
CD4 count	24	64	137	88.08±22.8	519.84	−1.84	0.07
<200	78	41	179	99.05±33.07	1093.62		
>200							

LDL: Low-density lipoprotein, SD: Standard deviation

Table 5: Mean HDL and CD4 count

HDL	*n*	Minimum	Maximum	Mean±SD	Variance	*t*-value (*t*-test)	*P*-value
CD4 count	24	17	70	31±14.25	203.06	−3.9	0
<200	78	24	75	43.31±10.8	116.64		
>200							

HDL: High-density lipoprotein, SD: Standard deviation

Table 6: Multivariate regression model for CD4 count and lipid profile

Lipid profile	Impact/beta coefficient	*P*-value
TC	−0.699	0.0001
TG	0.120	0.289
HDL	8.77	<0.0001
LDL	0.391	0.387

TC: Total cholesterol, LDL: Low-density lipoprotein, TG: Triglycerides, HDL: High-density lipoprotein

TC has a negative impact on the CD4 counts, whereas HDL has a positive impact on the CD4 counts.

This study has limitations while considering sample size, which is small. We evaluated patients on a group of drugs (first-line regimen of NNRTI) individual drugs in first-line NNRT-based regimen and their effect on lipid profile did not evaluate. In HIV patients, other drug intakes for opportunistic infections are common. Such drug's effect on lipid profile did not evaluate.

CONCLUSION

A total of 102 patients were included in the study. Patients were distributed from age 20 to 56 years with mean age of 37.12 years. Majority of the population were in between 35 and 41 years of age. Out of 102 patients, 28 patients (27%) were female and 74 patients were male (73%). In this sample, female's CD4 counts were better than male's which showed better drug compliance among females than males.

Patients were grouped into 2 categories based on CD4 count (<200/>200). Lipid profile of these patients in 2 groups evaluated separately. Mean value of HDL is not same among the patients with CD4 <200 and CD4 >200. Showed significant difference in the mean HDL among both categories of CD4 Count. Correlation analysis shows HDL that has a significant impact in predicting the CD4 counts.

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