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Original Research

Lipoproteins and C- Reactive Protein Abnormalities in HIV Positive Patients and their correlation with CD4 Cell Counts

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ABSTRACT
Aims-The study has been carried out to find the any correlation between changes in Lipoproteins and C - reactive protein with CD4 cell counts in HIV Positive patients. **Materials and methods**- The study was conducted at Department of Medicine, Pt. J. N. M. Medical College And Dr. B. R. Ambedkar Memorial Hospital, Raipur during the period of September 2012 to October 2013 on 100 HIV positive patients, of which 62 were males and 38 were females. Lipid profiles, C-reactive protein, CD4 cell count and other routine investigations were also done for all the patients. **Results-** In this study, of 100HIV positive patients, are grouped according to the CD4 cell counts in four groups, group I CD4 count <200/µL, group II CD4 count 201-350/µL, group III CD4 count 351-500/µL, and group IV has CD4 count>500/µL. Most patients with decreased CD4 count were found increased CRP level. Shows there is significant inverse correlation between CRP and CD4 count, as there is CD4 count decreases, the CRP level increases. It indicates as increase in severity of HIV infection associated with reduction in CD4 count, CRP level increases. We also observed serum level of total cholesterol, High density lipoprotein, were found to be decreased in HIV positive patients and on the other hand, the level of Very low density lipoprotein is increased as there is reduction of CD4 cell count. There is no significant change found in serum Triglycerides and low density Lipoprotein in relation with CD4 cell count. **Conclusion-** In the present study, lipid profile and C-reactive protein was altered in HIV positive patients with decreased CD4 count. Monitoring of lipid profile and C-reactive protein can be a good index of disease progression, management and cardio vascular risk assessment in HIV/AIDS patients in the absence of CD4 cell count facility.
Key words: HIV, AIDS, CD4 cell count, C-reactive protein, Lipoproteins, lipid profile.

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INTRODUCTION

Acquired immunodeficiency syndrome (AIDS), is a fatal illness, caused by the retrovirus called as human immune-deficiency virus, which breaks down the body's immune system, infects CD4 cells initially and leaving the victim vulnerable to a host of life threatening opportunistic infections, neurological disorders, or unusual malignancies.[1] AIDS is caused by the human immune-deficiency virus HIV-1, HIV-2. HIV infection /AIDS is a global and endemic, reported from every country. India has a population of one billion, around half of whom are adults in the sexually

active age group and more than 5 million persons living with HIV. The transmission route is still predominantly sexual. However, the distribution of HIV/AIDS in India is not uniform.[2] In Chhattisgarh, HIV prevalence was 0.17%. (NACO) The CD4+ T lymphocytes are the crucial cells in the orchestral events informing immune response to the foreign antigen and it is also the primary target cells for human immunodeficiency virus (HIV). The progressive loss of these cells eventually results in the loss of an ability to mount desirable immune response to any pathogen and death of the patients in the terminal stage of HIV infection, i. e., acquired immune deficiency syndrome (AIDS). The monitoring of CD4+ counts is used as a surrogate marker for HIV disease progression and effectiveness of anti retroviral treatment and follow-up of HIV positive patients.[3,4]

Recent data suggest that India harbors more than 5 million HIV positive patients and the rate of spread of disease is alarming. The prevalence is also increasing among patients with sexually transmitted infections (STIs). The clinical latency in the immune-compromised patients hinders follow up and management of the HIV disease. India, due to its limited resources, scarce facilities and economic constraints, can hardly afford wide use of viral load assays as marker of the disease status.[5] In these circumstances, estimation of accurate absolute counts of CD4+ and CD8+ cells and their ratios is an answer to the problem, as the CD4 counts are the principal surrogate marker in assessing the degree of immune deficiency in HIV infected persons. CD4+ T-lymphocyte levels are also used to categorize HIV related clinical conditions by CDC's classification system for HIV infection and expanded surveillance case definition for AIDS among adolescents and adults.[6]

Further, staging of HIV disease, its progression, response to Anti retroviral therapy (ART) and making decisions about initiation of chemoprophylaxis for opportunistic infections, are all based on CD4 counts.[7] HIV Infection can increase plasma triglyceride (TG) levels by decreasing the clearance of circulating lipoproteins, a process considered to be the result of reduced lipoprotein lipase (LPL) or by stimulating hepatic lipid synthesis through increases in either hepatic fatty acid synthesis or reesterification of fatty acid (FA) derived from lipolysis.[8] Hyper triglyceridaemia was the first dyslipidemia to be reported in HIV infected patients, but other lipid abnormalities such as hypo-cholesterolaemia or hypo HDL cholesterolaemia have also been reported. Metabolic disturbances in the HIV- infected patients are incriminated to be risk factors of accelerated atherosclerosis and cardio vascular diseases due to altered lipid metabolism.[9]

In view of the increasing incidence of HIV infection throughout the world the present study was undertaken to find out any correlation between the changes in lipid profile and the different clinical stages of HIV infection.[10]

CRP is an acute phase protein whose levels increase with the infection and inflammation. CRP is an important component of the innate immune system, which is synthesized in the hepatocytes, primarily in response to IL-6 and other cytokines. CRP levels increases with infection and there exists a negative correlation between CRP and CD4 count. Elevated levels of CRP can usually be demonstrated in case of acute myocardial infarction, rheumatoid arthritis, bacterial and viral infections, acute rheumatic fever, with or without carditis, and in several types of malignancies, particularly those with metastasis. HIV is a progressive infection accompanied by destruction of the immune system largely through depletion of CD-4 cells.[9,11]

As a result immune system is affected and CD4 count is decreased giving rise to opportunistic infections, which result in acute inflammation and release C-reactive proteins. However, during an inflammatory response or infection, the levels of C-RP may increase by as much as 1000 fold. This increase in C-RP level may be detected as early as 5-10 hrs after tissue damage. As HIV infection leads too many opportunistic infections, inflammation occurs generally which leads to increase in C-RP level and decrease in CD4 count. At present CD4 count and HIV-RNA assay are potent markers of prognosis of HIV infection. But measurement of HIV-RNA level is highly expensive and is not used in most hospitals.[12] As CD4 count is not most cost effective; the study of C-RP in relation to opportunistic infections is aimed to evaluate the role of CRP as a diagnostic and prognostic indicator of opportunistic infection. It has been suggested that the measurement of CRP levels may be an inexpensive method for the study of prognosis of HIV infection and can be used as a vital tool to monitor the anti-retroviral therapy and can be used as a marker of degree of immune suppression thus a decreased level of CRP is thus an indicator of good treatment response to the underlying infection and Lower levels of CRP have been shown to predict longer survival within HIV- infected individuals. CRP may have arolein monitoring HIV-infected patients in regions where anti retroviral therapies are becoming available but where frequent monitoring with viral loads and CD4 counts is still cost prohibitive.[13] Patients with HIV demonstrate increased rates of coronary heart disease compared with patients without HIV. Although traditional cardiovascular risk factors have been shown to be common among patients with HIV, the role of inflammation and the utility of related biomarkers have not been studied. In the general population, there is

strong evidence that inflammation plays a role in the development of acute myocardial infarction (AMI), and elevated levels of C-reactive protein (CRP) have been significantly associated with coronary events in a number of studies. CRP levels have been shown to be elevated in patients with HIV compared with general populations.[14] However, it remains unknown whether CRP adds prognostic information with respect to cardiovascular events in the HIV population. The present study was undertaken to find out the relationship between changes in CD4 cell count, lipoproteins and C-reactive protein in HIV positive patients.

To evaluate the effect that Human Immuno-deficiency Virus infection and the progression of AIDS have on lipids profile and C-reactive protein, we measured the plasma concentrations of total cholesterol, LDL cholesterol, HDL cholesterol, VLDL cholesterol and triglycerides, C reactive protein, in HIV positive patients with or without secondary inflammatory acute disease, and then determined their relation with CD4 cell lymphocyte counts as cellular immune markers.

MATERIALS AND METHODS

Study Population– The study was carried out at department of medicine, Dr. B. R. A. M. Hospital Raipur (C.G.) with 100 HIV positive adult patients whether symptomatic or asymptomatic, attending outdoor or admitted in male and female ward and attending at the ART centre of dept. of medicine, Dr. B. R. A. M. Hospital, Raipur (C.G.) during the study period September 2012 to October 2013 and gave oral informed consent after understanding of the purpose of study.

Sample collection– The blood sample collected under usual precautions. For accurate comparison to normal established normal values, fasting morning blood sample should be collected. Venous blood should be collected from the participant patient by clean vein puncture and collected into a simple clean dry glass vials without additive or anticoagulants and samples are allowed to clot for serum sample, and centrifuged the specimen sample to separate the serum or plasma from the cells, are used for the analysis in laboratory. HIV testing-For diagnosis and confirmation of HIV infection we followed NACO recommendations for HIV testing, By SD Bioline Rapid card, Triline, and Trispotcard test. SD Bioline HIV1/23.0 is an immune-chromatographic rapid test for the qualitative detection of all anti bodies of all is types (IgG, IgM, IgA) specific to HIV–1 including subtype and HIV-2 simultaneously, in human serum, plasma or whole bloods. CD4 cell count-Was estimated by FACS (Fluorescence activated cells otter) count System (Becton Dickinson, USA). Single Plate form Flow cytometry method. Lipid profile analysis-Serum total cholesterol, triglycerides, HDL-C, LDL-C, VLDL-C were estimated by a fully automated chemical analyzer machine (I-lab 650) by enzymatic method. C-reactive protein analysis- CRP test was done by nephalometry method using the automatic machine (IMMAGE 800).

Statistical analysis- All data were expressed as mean±SD. Microsoft excel for window 2010 was used for statistical analysis.

RESULTS

This study of 100 HIV positive patients were selected out of which 68 were male and 32 were female. The mean age limit was 35.18 SD±8.69 in HIV positive patients. Out of 100 patients 62 were males and 38 were female. Most of the patients were male and in age group of 15 to 45 years. 100 HIV positive patients, are grouped according to the CD4 cell counts in four groups, group I CD4 count< 200/µL, group II CD4 count 201-350/µL, group III CD4 count 351 -500/µL, and group IV has CD4 count> 500/µL.

Table 1 shows the distribution of CRP in correlation with CD4 cell counts in HIV positive patients. In this study group of 100 HIV Positive patients, mean CRP was 31.36±40.22. Patients with CRP<3mg/L was 10% and patients with CRP> 3was 90%. Most patients has increased CRP level> 3mg/L. Shows the HIV infection is associated with increased CRP level. There is significant inverse correlation found between CRP and CD4 count, as there is CD4 count decreases, CRP level increases. It indicates as increase in severity of HIV infection CD4 count decreases and CRP level increases.

Table 2. shows the distribution of total cholesterol in correlation with CD4 cell counts in HIV positive patients. In this study, mean total cholesterol was 142.17±41.73, out of 100 HIV positive patients, 33 patients has TC<150mg/dl with CD4 count <200/µL, 15 patients has TC <150mg/dl with CD4 count<201-350/µL, 8 patients has TC <150mg/dl with CD4 count 350-500/µL and 7 patients has TC <150mg/dl with CD4 count>500/µL. Total 63 HIV positive patients were found with decreased serum Total cholesterol level. So HIV infection is associated with decreased serum TC level. As CD4 count decease there is decreased serum total cholesterol level occurs.

The distribution of VLDL-C in correlation with CD4 cell counts in HIV positive patients was calculated. In this study, mean VLDL-C 47.02±23.14. out of 100 patients, 32 patients has VLDL-C >35mg/dl with CD4 cell count<200/µL, 17 patients has VLDL- C>35mg/ dl with CD4 cell count 201-350/µL, 9 patients has VLDL-C >35mg/dl with CD4 cell count 351-500/µL, 6 patients has VLDL- C >35mg/dl with CD4 cell count >500/µL, total 64 patients has increased level of VLDL-C level. Most of the patients has found with increased VLDL-C

level. There is inverse correlation is found between the VLDL-C level and CD4 cell count, as CD4 cell count Decreases VLDL– C level also increases. In this study, mean TGs was 136.29±72.98. The maximum number of patients shows normal level of TGs, so there is no significant change found in TGs in relation with CD4 cell count. In this study, mean LDL-C was 78.88±31.20. The maximum number of patients showed normal level of LDL-C so there is no significant change found in LDL-C in relation with CD4 cell count.

Table1: Distribution of C-reactive protein in correlation with CD4 count

CRP mg/L	CD4 Cells/ml								Total	
	<200		201-350		351-500		>500			
	n	%	N	%	n	%	n	%	n	%
<5	2	2	6	6	5	5	6	6	19	19
6-10	11	11	4	4	2	2	-	-	17	17
11-20	14	14	10	10	2	2	2	2	28	28
21-30	7	7	1	1	-	-	-	-	8	8
31-40	2	2	-	-	1	1	-	-	3	3
41-50	3	3	1	1	1	1	-	-	5	5
>50	17	17	3	3	-	-	-	-	20	20
TOTAL	56	56	25	25	11	11	8	8	100	100

Mean CRP 31.36 SD±40.22

Table 2: distribution of total cholesterol in correlation with CD4 cell Count

CD4 Cell Count/µL	No of patients Total cholesterol - mg/Dl			Total
	150	151-200	>200	
<200	*33*	*20*	*3*	*56*
201-350	*15*	*9*	*2*	*26*
351-500	*8*	*2*	-	*10*
>500	*7*	*1*	–	*8*
TOTAL	*63*	*32*	*5*	*100*

Mean total cholesterol 142.17SD± 41.73

Table 3: Distribution of HDL-C in Correlation with CD4 Cell Count

CD4 Cell Count/µL	No of patients HDL- Cog/dl		Total
	<30	31-60	
<200	32	24	56
201-350	13	14	27
351-500	3	6	9
>500	3	5	8
TOTAL	51	49	100

Table 4: Distribution of VLDL-C in correlationwithcd4cellcount

CD4 Cell Count/µL	No. of patients VLDL-Cmg/dl		Total
	1-35	>35	
<200	24	32	56
201-350	10	17	27
351-500	-	9	9
>500	2	6	8
Total	36	64	100

Mean VLDL-C 47.02 SD±23.14

DISCUSSION

Analysis of CRP in correlation with CD4 cell count: In this study there is inverse correlation found between CRP and CD4 count, as there is CD4 count decreases, CRP level increases.

The importance of CRP as inflammatory markers: This study is consistent with the extent of HIV disease progression and concurrent opportunistic infections present in the patients. In AIDS, opportunistic an infection develops by which the C-RP level changes. The C –RP appears useful for diagnosis and monitoring of inter-current infection in HIV-1 antibody positive patients.[14] A clinically elevated CRP concentration was predictive of HIV disease progression and mortality. CRP may be an important and inexpensive prognostic indicator for HIV-infected patients, particularly in resource- poor settings individuals with progression to AIDS had higher CRP levels than those without increased CRP. In addition, anti retroviral therapy was also independently associated with increased CVD risk.[15] CRP can be used as a marker for preclinical cardiovascular disease in HIV- infected patients. And may predict a higher risk of future coronary events in HIV- infected patients receiving ART. CRP might be a valuable adjunct to traditional risk factors in estimating overall cardiovascular risk in HIV infected patients on ART.[16]

The test is cost effective, easily available, does not need elaborate equipment and technical skill. It may not replace the CD-4 count in diagnosis as a whole, but ads up more information on the state of the patient. This study reveals that C-RP level serves as a good prognostic serological indicator in HIV or AIDS disease progression.[17]

Analysis of correlation between lipid profile in HIV positive patients and CD4 count: In this study, the fasting level of Total cholesterol, Triglycerides, HDL-c, LDL-c, VLDL-C of HIV positive patients are evaluated and also assessed were the CD4 count of all patients. To assess the effect of immunological changes due to the HIV infection and its impact on lipid profiles, the HIV positive subjects were grouped into 4 levels based on CD4 cell count. Group I<200/µL, group II 201-350/µL, group III 301-500/µL, group IV>500/µL. Camara, M. et al in 2010, depicted the similar results as mentioned in our study.[18]

A significant positive correlation was found between TC, HDL-C and the CD4 cell level of HIV positive subject. This is instructive that as the infection progress with drop in CD4 cell count there is drop in TC and HDL- C level of these subject. A higher CD4 count in the HIV- positive subjects was associated with higher TC and HDL-C while a lower CD4 count was associated with higher VLDL-C levels. A low HDL-C concentration increases the risk for coronary artery disease in HIV- infected patients. And no significant association was found between TGs and CD4 cells and LDL- C and CD4 cells. Hernandez, J. et al also found similar results in 2016.[19]

The earlier study showed that the lipid profile was altered in HIV positive patients. Alteration in lipid profile occurred even in early stages of HIV infection and more so as the disease progressed. Previous studies also have demonstrated that HIV positive patients exhibits highly abnormal lipid profile in plasma with increase in immunological deficiency, decreased CD4 cell count and development of AIDS lipid profile disorders–indicated by and increased level of Total cholesterol and HDL- C and increased level of VLDL-C level. This study also showed similar findings with earlier reports as Hernandez, J. et al in 2016.[19] These changes were proportional to the lowering of CD4 cell count, which reflected this variety of HIV disease progression. The increase in triglyceride catabolism in relation to a reduction of lipoprotein lipase (LPL) activity was responsible for these lipid changes. Guardo, A. C., in 2015 concluded the same hypothesis.[20] Hence it may be suggested that the lipid profile measurement can be a good index of HIV disease progression in HIV/AIDS patients. HIV infection has itself a profound impact on lipid and lipoprotein metabolism that is further influenced by anti retroviral drugs. HIV infection and its treatment are associated with dyslipidemia, and increased risk of cardiovascular disease.

In conclusion atherogenic lipid VLDL- C, have been found to increase as the CD4 cells decrease and level of good cholesterol HDL-C reduces significantly as the disease progress with lower CD4 cells count, were at the higher risk of coronary heart disease. So the lipid profile can therefore be a good index of disease progression in HIV/AIDS patients there is need for proper check on lipid profile as the CD4 cell count reduces in HIV infected patients. This will help the doctor to decide on the type of ART to administer to the patient ascertain combination of these drugs increase the level of these atherogenic lipid level. HIV- infected patients receiving WHO-recommended first-line HAART have a high prevalence of lipid profile derangements. Uses of first-line HAART regimens are significantly associated with atherogenic lipid profile. Therefore, the findings indicate that need to assess lipid profiles at baseline before initiation of HAART treatment and lipid profile monitoring during therapy to monitor any rising trends. The present study showed that the lipid profile was altered in HIV infected and AIDS patients. Alternation in the lipid profile occurred even during the early stages of HIV infection and more so as the disease progressed. Previous studies have demonstrated that patients with AIDS exhibit highly abnormal total lipid concentration in plasma (Holzer, M., S. et al and Bartelt, A. C. et al in 2017).[21,23] A few

authors have determined the level of plasma triglycerides, total cholesterol and HDL–C in HIV infected individuals by the level of immunological deficiency according to the CD4 count, and they also came into same conclusion, with an increase in immunological deficiency and clinical development of HIV infection, lipid profile disorder indicated by an increase in TGs and decreased in concentration of HDL-C.[24]

Our study also consistent with earlier reports, this study also showed similar findings in which the decrease in CD4 count due to HIV disease progression was accompanied by a decrease in total cholesterol, HDL-C and increase in VLDL-C level. This is a matter of great clinical importance, since dyslipidemia occurs commonly in HIV-infected patients and serum lipids predict CVD risk among patients receiving ART. Because ART-associated dyslipidemia involves abnormalities of several lipid fractions, and components of ART have differing effects on lipids that vary within and between ART classes, assessing the magnitude of CVD risk associated with ART has been challenging, as has understanding its pathophysiology and implications for therapy.

This emphasizes the importance of educating physicians to test patients 'baseline serum lipid profiles before administration of ART, particularly PIs.

CONCLUSION

The increased CRP is very sensitive marker of infection and inflammation in HIV and can be identify opportunistic infection at the earliest. C-reactive protein can be used as an indicator for the treatment response in HIV positive patients. Elevated CRP and HIV are independently associated with increased risk of acute myocardial infection. Increased CRP have a markedly increased risk of AMI. So the measurement of CRP may be useful in the cardio vascular risk assessment in HIV infection. The test is cost effective, easily available, does not need elaborate equipment and technical skill. It may not replace the CD-4 count in diagnosis as a whole, but ads up more information on the state of the patient. This study reveals that C-RP level serves as a good prognostic serological indicator in HIV or AIDS disease progression and independent predictor of mortality in HIV infected patients.

HIV infection has itself a profound impact on lipid and lipoprotein metabolism that is further influenced by anti retroviral drugs. HIV infection and its treatment are associated with dyslipidaemia and increased risk of cardiovascular disease. In conclusion atherogenic lipid VLDL-c, have been found to increase as the CD4 cells decrease and level of good cholesterol HDL-c reduces significantly as the disease progress with lower CD4 cells count, were at the higher risk of coronary heart disease. In the present study, lipid profile and C-reactive protein was altered in HIV positive patients. Monitoring of lipid profile and C-reactive protein can be a good index of disease progression, management and cardiovascular risk assessment in HIV/AIDS patients in the absence of CD4 cell count facility. CRP can be used as indicator of inflammation and associated opportunistic infection in HIV/AIDS patients, used to monitor response to anti retroviral therapy. So lipid profile and C-Reactive protein should be measured routinely in all HIV positive patients.

REFERENCES

1. Adewole O, EzeS, Betiku Ye, Anteyi E, WadaI, Ajuwon Z, Erhabor Lipid profile in HIV/AIDS patients in Nigeria African Health Sciences 2010; 10 (2): 144–149.
2. Afsoon D., Roberts, Richard A. Muesing, David M. Parenti, Judy Hsia, Alan G. Wasserman, and Gary L. Simon Alterations in Serum Levels of Lipids and Lipoproteins with Indinavir Therapy for Human Immunodeficiency Virus- Infected Clinical Infectious Diseases 1999; 29: 441–3.
3. Agete Tadewos et al, Prevalence of dyslipidaemia among HIV-infected patients using first line highly active anti retroviral therapy in Southern Ethiopia: across-sectional comparative group study.
4. Owens R.J., Anantharamaiah G.M., Kahion J.B., et al. Apolipoprotein A1 and its amphipathic helix peptide analogues inhibit human immunodeficiency virus-induced syncytium formation. J Clin Invest 1990; 86:1142-50.
5. Feingold K.R., Memon R.A., Moser A.H., Grunfeld C. Paraoxonase activity in the serum and hepatic mRNA levels decrease during the acute phase response. Atherosclerosis 1998;139:307-15.
6. McLemore J.L., Beeley P., Thorton K.,et al. Rapid automated determination of lipid hydroperoxide concentrations and the total antioxidant status of serum samples from patients infected with HIV: elevated lipid hydroperoxide concentrations and depleted total antioxidant capacity of serum samples. Am J Clin Pathol 1998;109:268-73.
7. Favier A., Sappey C., Leclerc P., et al. Antioxidant status and lipid peroxidation in patients infected with HIV. Chem Biol Interact 1994;91:165-80.
8. Feingold K.R., Memon R.A., Moser A.H., et al. Endotoxin and interleukin-1 decrease hepatic lipase mRNA levels. Atherosclerosis 1999;142:379-87.
9. Monnet D., Kacou E., Gershey Damet G.M., et al. Inflammatory reaction markers and nutritional markers in HIV Infection. Ann Biol Clin 1991;49:428-32.
10. Akira S., Kishimoto T. IL-6 and NF-IL6 in acute-phase response and viral infection. Immunol Rev 1992;127:25-50.
11. Barcellini W., Rizzardi G.P., Borghi M.O., et al TH1 and TH2 cytokine production by peripheral blood mononuclear cells from HIV-infected patients. AIDS 1994;8:757-62.
12. Wigmore S.J., Featon K.H.C., Maingay J.P. Interleukin-8 can mediate acute-phase protein production by isolated human hepatocytes. Am J Physiol 1997;273:E720-6.

13. Fleck A., Raines G., Hawker F., et al. Increased vascular permeability: a major cause of hypoalbuminemia in disease and injury. Lancet 1985;1:781-4.
14. Asztalos, B. F., M. De La Llera-Moya, G. E. Dallal, K. V. Horvath, E. J. Schaefer, and G. H. Rothblat. 2005. Differential effects of HDL subpopulations on cellular ABCA1- and SR-BI-mediated cholesterol efflux. J. Lipid Res. 46: 2246–2253.
15. El-Sadr, W. M., C. M. Mullin, A. Carr, C. Gibert, C. Rappoport, F. Visnegarwala, C. Grunfeld, and S. S. Raghavan. 2005. Effects of HIV disease on lipid, glucose and insulin levels: results from a large antiretroviral-naive cohort. HIV Med. 6: 114–121.
16. Claudio, C. C., R. V. Patin, C. Z. Palchetti, D. M. Machado, R. C. Succi, and F. L. Oliveira. 2013. Nutritional status and metabolic disorders in HIV-exposed uninfected prepubertal children. Nutrition. 29: 1020–1023.
17. Suy, A., P. Castro, M. Nomdedeu, F. García, A. López, E. Fumero, T. Gallart, L. Lopalco, O. Coll, J. M. Gatell, et al. 2007. Immunological profile of heterosexual highly HIV-exposed uninfected individuals: predominant role of CD4 and CD8 T-cell activation. J. Infect. Dis. 196: 1191–1201.
18. Camara, M., T. Ndiaye Dieye, M. Seydi, A. Aziz Diallo, M. Fall, P. Alassane Diaw, P. Salif Sow, S. Mboup, L. Kestens, W. Jennes, et al. 2010. Low-level CD4+ T cell activation in HIV-exposed seronegative subjects: influence of gender and condom use. J. Infect. Dis. 201: 835–842.
19. Hernandez, J. C., G. St Laurent, and S. Urcuqui-Inchima. 2016. HIV-1-exposed seronegative individuals show alteration in TLR expression and pro-inflammatory cytokine production ex vivo: An innate immune quiescence status? Immunol. Res. 64: 280–290.
20. Guardo, A. C., M. Ruiz-Riol, E. Fernández, M. J. Maleno, M. E. Bargalló, A. León, N. Climent, F. García, J. M. Gatell, C. Brander, et al. 2015. Detection of HIV-1-specific T-cell immune responses in highly HIV-exposed uninfected individuals by in-vitro dendritic cell co-culture. AIDS. 29: 1309–1318.
21. Holzer, M., S. Kern, M Trieb, A. Trakaki, and G. Marsche. 2017. HDL structure and function is profoundly affected when stored frozen in the absence of cryoprotectants. J. Lipid Res. 58: 2220–2228.
22. Funderburg, N. T., and N. N. Mehta. 2016. Lipid abnormalities and inflammation in HIV infection. Curr. HIV/AIDS Rep. 13: 218–225.
23. Vaisar, T., C. Tang, I. Babenko, P. Hutchins, J. Wimberger, A. F. Suffredini, and J. W. Heinecke. 2015. Inflammatory remodeling of the HDL proteome impairs cholesterol efflux capacity. J. Lipid Res. 56: 1519–1530.
24. Bartelt, A., C. John, N. Schaltenberg, J. F. P. Berbée, A. Worthmann, M. L. Cherradi, C. Schlein, J. Piepenburg, M. R. Boon, F. Rinninger, et al. 2017. Thermogenic adipocytes promote HDL turnover and reverse cholesterol transport. Nat. Commun. 8: 15010.