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Trends of Serum Highly Sensitive C-reactive protein and Albumin Status in HIV Patients

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Abstract: Immune activation has been proved as a significant contributing factor to HIV disease progression. Serum hs-CRP increase and albumin decrease in HIV infected individuals as a response of immune activation through cytokines. In this study we estimated serum hs-CRP and albumin levels and hs- CRP /Albumin ratio in HIV seropositive and control groups. This is a case control study having 40 HIV patients with age, sex matched 40 controls. In our study we observed statistically significant difference in serum hs-CRP, albumin and hs-CRP /Albumin ratio in HIV seropositive compared to control group ($p<0.001$).This made us to propose that serum hs-CRP , albumin and hs CRP /Albumin ratio can be used as prudent prognostic markers in HIV infection and predictor of mortality.

Keywords: Human immunodeficiency virus, high sensitive- C-reactive protein, albumin.

INTRODUCTION

Human immunodeficiency virus (HIV) infection is said to be hyper-inflammatory. Inflammation is an early immune response to injury which involves host cells, blood vessels and proteins. It has been observed that anti-retroviral therapy used in HIV infections have limitations to fully counteract inflammation. Infection with HIV falls in to dysregulation of the cytokine profile. Cytokines are vital in controlling the homeostasis of the immune system [1]. Acute-phase proteins are group of plasma proteins that increase or decrease in response to inflammatory stimuli such as infections, trauma, and neoplasm. This response is mediated by cytokines such as interleukin-6, IL-1, tumor necrosis factor-alpha [2].

The acute phase proteins such as C-reactive protein (CRP) increases markedly in response to infection, and the magnitude of the increase may correlate with the severity of the infection. On the other hand albumin the other acute phase protein is a potent prognostic marker of outcomes in infection-related disease and its level decrease in response to infections. Successful management of HIV patients requires thorough monitoring of several factors [3]. Few studies have focused on role of serum albumin and C-Reactive Proteins in HIV infection [4, 5]. Recently, the hs-CRP/Albumin ratio was recognized as a novel inflammatory indicator in infectious disease [6]. Considering this, we further studied levels of serum albumin and serum hs- CRP along with hs-CRP /Albumin ratio in HIV patients on anti-retro viral therapy.

MATERIALS AND METHODS

This study was carried out in Government Grant Medical College and Sir JJ Group of Hospitals Mumbai. This case control study was approved by the Institutional Ethical Committee and National AIDS Control Organization New Delhi. The patients visiting Centre of Excellence of HIV/AIDS, Sir JJ Group of Hospitals Mumbai were incorporated in the study. Overall 80 subjects from both genders were enrolled in this study. The subjects were of age from 17 to 55 years from diverse socioeconomic background. The study design was explained and written consent from all the subjects was acquired. The subjects were divided into one group having 40 HIV seropositive patients on antiretroviral therapy and other, control group having 40 HIV seronegative subjects. The patients having recent history of pre renal, pre hepatic dysfunction and burn were excluded from the study. For analytical

purpose, blood samples were collected in plain red top vacuum tube. Samples were centrifuged after two hours of collection and pooled serum was stored at -20^0C. The high sensitivity CRP (hs-CRP) measurements can more accurately detect lower concentrations of the protein as compared to CRP. The estimation of serum hs-CRP was carried out by chemiluminescence method on Siemens-model Immulite 1000. Serum albumin was estimated by BCG method on fully auto analyser. Based on the outcome of serum hs-CRP and serum albumin levels, the hs-CRP /Albumin ratio was calculated. Statistical analysis was carried with SPSS Software with suitable statistical tests.

RESULT

It is observed that serum hs-CRP levels are 61.74 ±42.43 mgs/dl and 2.72 ±1.05 mgs/dl, Serum albumin levels are 4.23 ±0.37 gms/dl and 4.51 ±0.27 gms/dl, hs- CRP/albumin ratio is 14.76±10.26 and 0.61±0.24 in HIV seropostive group and control group respectively. The difference between HIV seropositive and control group is statistically significant in all the three variables (p value <0.001).

Table-1: Serum hs- CRP and albumin and its ratio in HIV Seropositive and Control group

	hs -CRP mgs/dl mean ±SD	Albumin gms/dl mean ±SD	hs- CRP /Albumin ratio mean ±SD
HIV Seropositive Group n=40	61.74 ±42.43	4.23 ±0.37	14.76±10.26
Control Group n =40	2.72 ±1.05	4.51 ±0.27	0.61±0.24
Independent T test	8.797**	3.817**	8.723**
P value	<0.001	<0.001	<0.001
Significant at 5% level	Yes	Yes	Yes

** Statistically highly Significant at 0.01% level i.e., P<0.001

DISCUSSION

HIV like inflammatory condition is associated with changes in the expression of various endogenous soluble proteins. These may be directly involved in pathogenic processes or be simple outcomes of such processes. What so ever may be the causative relationship, proteins that display altered expression during disease can be useful as biomarkers for better understanding of pathogenic processes. Thus, some of these biomarkers can help to predict a patient's clinical course and/or response to therapy. HIV infection is associated with persistent enduring immune responses and progressive immunopathology. These processes increasingly generate soluble markers related to innate and adaptive immune activation [7].

In human immunodeficiency virus infection, the release of cytokines triggers and modulates systemic acute phase reaction and hepatic acute phase proteins. C - reactive protein was first identified by Tillett and Francis in 1930. It was so named because it was a substance in the serum of patients with acute inflammation that reacted with the C (capsular) -polysaccharide of pneumococcus. In human. C - reactive protein is composed of five identical polypeptide units noncovalent arranged as a cyclic pentamer around a Ca-binding cavity. It contains 224 amino acid residues. C-reactive Proteins levels rise noticeably during inflammatory processes in the body. CRP binds to phosphoryl choline on microbes. It is considered to assist incomplete binding to foreign and damaged cells. The cell boosts phagocytosis by macrophages which express a receptor for CRP. It is also assumed to have an important role in innate immunity, as an early defense system against infections [8, 9]. Most of the CRP is produced from liver in response to interleukin 6 produced from macrophages and adipocytes. Hs-CRP is considered to be a potential biomarker for predicting disease progression and cardiovascular disease risk, which seems to be one of the major long-term complications in HIV patients [10]. Serum Albumin is one of the major plasma proteins synthesized in liver. It has a molecular weight 67 k Da .It has important role as an antioxidant, transport protein and in maintenance of osmotic balance between intravascular and interstitial spaces. It has a longer half-life as compared to other proteins [11].The various studies have focused on the role of serum albumin in progression of HIV Infection [12, 13]. In the present study we observed significant difference in serum albumin and serum hs-CRP levels as compared to control. These findings are in agreement with earlier studies [14, 15].The level of highly sensitive C-reactive protein increases markedly in response to infection and may correlate with the severity of the infection. Albumin is also said to be a potent prognostic marker of outcomes in infection-related disease such as HIV. Its levels are found to be decreased during the response to acute phase infections. Based on these properties, we speculated that the ratio of hs-CRP to albumin could be used as a prognostic marker, as has been observed in some other inflammatory diseases [16, 17]. Serum albumin level seems to be linked with the chronic nature of disease, and represent the inflammatory status. Its predicting outcomes in chronic and inflammatory diseases are acknowledged. Nevertheless, decrease in serum albumin may be the result of infection. In evaluating patients with varying causal conditions, this marker alone may create bias because albumin levels can be affected by chronic nutritional and inflammatory status also. Thus, instead of analyzing a single factor on its own, the levels of hs-CRP and albumin were

combined. The amalgamation of these prognostic markers eases inflammatory and nutritional factors to be merged. Thus, the hs-CRP/Albumin ratio may be an indicator of a better inflammation response. In the present study, we have found statistically significant difference in hs-CRP/albumin ratio in HIV patients as compared to that of control.

CONCLUSION

We conclude that serum hs- CRP and albumin with its ratio appears to be prudential markers of HIV progression. Furthermore potential studies with larger populations at different stages of HIV infection are necessary to precisely evaluate the hs-CRP/Albumin ratio as a prognostic marker and predictor of mortality.

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