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To Assess Some Special Plasma Proteins in HIV Positive Patients

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Abstract

Acquired Immunodeficiency Syndrome (AIDS) has become the focus of much global concern and that is reaching epidemic proportions in some parts of the world. Infection with human immunedeficiency virus is a progressive condition which may cause endothelial dysfunction and liver damage leading to coagulopathy. With adventure of highly active antiretroviral therapy (HAART), life expectancy has prolonged in HIV positive patients but several acquired immunodeficiency syndrome (AIDS)-related conditions such as coagulopathies are responsible for associated morbidity and mortality. C - reactive protein (CRP) is a highly sensitive marker of infection and inflammation and its level increase with infection. Therefore, the aim of the study was to assess some special proteins in HIV positive patients. **Aim**: **1)** To determine the concentration of serum C-reactive protein, fibrinogen, total proteins, albumin and A/G ratio in HIV positive patients & in age matched healthy controls. **Study Design:** Case control study. **Setting:** HIV positive patients from SCSM General Hospital Solapur. **Participants:** 80 clinically diagnosed HIV positive patients on ART and 41 normal subjects were recruited as control. **Results:** Serum C-reactive protein and fibrinogen was significantly increased ($P<0.01$) in HIV positive patients on ART as compared to controls. Serum total proteins and albumin levels were decreased significantly ($P<0.01$) in HIV positive patients on ART as compared to controls. **Conclusion:** Fibrinogen and CRP is the major component of acute phase proteins. Estimation of CRP is important for the evaluation of acute phase response. It is also useful for prognostic and can be used as an early marker of HIV infected patients.

Keywords: C- Reactive Protein (CRP), fibrinogen, total proteins and albumin Albumin/Globulin (A/G) Ratio.

INTRODUCTION

HIV is the human immunodeficiency virus belonging to class of Retroviruses and sub family Lentiviridae. It is rapidly mutating virus. The acquired immunodeficiency syndrome (AIDS) is a fatal illness caused by a retrovirus known as the human immunodeficiency virus that breaks down the body's immune system, infects CD^{4+} cells initially and progressively leads to AIDS. This disease is characterized by immunosupression, secondary neoplasm and neurological manifestations [1].

HIV continues to be a major global public health issue. In 2016, an estimated 36.7 million people were living with HIV with a global HIV prevalence of 0.8% among adults [2, 3]. Since the start of epidemic, an estimated 78 million people have become infected with HIV and 35 million people have died of AIDS related illnesses. In 2016, 1 million people died of AIDS related illnesses [4].

Acquired Immunodeficiency Syndrome (AIDS) has become the focus of much global concern and that is reaching epidemic proportions in some parts of the world [5].

CRP is a β – globulin and can stimulate complement activity and macrophage phagocytosis. Interleukins (IL), especially IL-1 and IL-6 released by macrophages and lymphocytes, are the primary agents which cause induction of release of these acute phase proteins [6]. High-sensitive C-reactive protein has been touted as a potential solution for both problems. First, hsCRP is considered to be a potential biomarker for predicting long - term disease progression of HIV patients. Second, it is also considered to be a marker for predicting mortality and as a tool for routine monitoring of disease activity with a potential to replace traditional costlier measures such as CD4 count.

Fibrinogen is a key component of the coagulation cascade and an acute phase reactant in progressed stages of HIV infection. Acute inflammation due to infection is one of the important causes of coagulation disorders [7]. Cytokines consists of tumor necrosis factor-α (TNF-α), Interleukin-1 (IL-1) and IL-6, act as mediators for activation of coagulation system [8, 9]. Vascular endothelial cells interacting with releasing cytokines from leukocyte, adhesion molecules and growth factors play an important role in up-regulation of coagulation system [10].

Estimating serum total proteins and albumin level assesses the nutritional status of the patients. Malnutrition is an important complication of HIV infection. Macronutrients such as proteins deficiencies may be common during human immunodeficiency virus (HIV) infection. Malabsorption, impaired synthesis, diarrhoea, impaired storage and altered metabolism can contribute to the development of macronutrient deficiencies [11].

Human immunodeficiency virus (HIV) infection is a major global health problem and nutritional disorders are often present in HIV positive patients. So the present study was aimed to assess the serum fibrinogen, C reactive protein, and nutritional status by determining the total proteins and albumin levels for better understanding the pathophysiology of disease and can be useful to monitor the disease progression.

MATERIALS AND METHODS

Present study was conducted in the Department of Biochemistry, Dr. Vaishampayan Memorial Government Medical College Solapur and SCSM. General Hospital Solapur.

We performed a case control study of 80 clinically diagnosed HIV positive patients on ART in the age group 20-50 years and 41 normal subjects were recruited as control.

Table No. 1: Serum plasma proteins level in HIV positive patients and control group.

Sr.No.	Lipid Profile	Mean	± SD	T value	P value
1	C-reactive protein (mg/dl)			12.57	P <0.01
	HIV Positive	4.57	± **1**.21		
	Control	2.12	± **0**.25		
2	Fibrinogen (mg/dl)			25.73	P <0.01
	HIV Positive	509.84	± 46.86		
	Control	284.73	± 40.36		
3	Total proteins (gm/dl)			21.16	P <0.01
	HIV Positive	5.99	± **0**.27		
	Control	7.21	± **0**.34		
4	Albumin (gm/dl)			9.38	P <0.01
	HIV Positive	3.1	±**0**.21		
	Control	3.61	± **0**.38		
5	A/G Ratio			16.58	P <0.01
	HIV Positive	1.0	± 0.16		
	Control	1.59	± 0.22		

P <0.01 Significant (Z Test & Paired t test)

Exclusion Criteria: Patients suffering from myocardial infarction, other malignancies, liver or kidney disease , patients with acute viral disease hepatitis A, E, Herpes virus, Mycobacterium tuberculosis, fever, cold, loss of appetite, loss of weight were excluded from this study.

In addition, a history of a familial dyslipidemia, patients receiving medications affecting lipid metabolism, such as lipid lowering drugs, were excluded from this study.

The Institutional Ethical Committee approved the study and Informed Consent was obtained from each participant in the study.

In the present study blood samples were collected under aseptic condition from control group and from HIV positive patients. Serum was separated and analyzed for C-reactive protein by turbidimetric method [12], fibrinogen by Fibroquant kit method [13], total proteins by Biuret method [14] and albumin by Bromocresol green method [15].

The results were expressed as means ± SD. Statistical analysis was done by using "Z test" and "Unpaired T test".

RESULTS AND DISCUSSION

The present study was focused on estimation of serum plasma proteins such as C-reactive protein, fibrinogen, total proteins, albumin and A/G ratio in HIV positive patients and healthy controls.

This study showed that some plasma proteins were altered in HIV positive patients compared to the controls (Table no 1). Serum C-reactive reactive protein and fibrinogen levels were significantly increased in HIV positive patients on ART as compared to controls ($P< 0.01$). Serum total proteins and albumin levels of HIV positive patients were significantly decreased in HIV positive patients on ART as compared to controls ($P< 0.01$). (Table no 1).

C-reactive protein (CRP) is a highly sensitive marker of infection and inflammation and its level increase with infection. It can stimulate complement activity and macrophage phagocytosis. Interleukins (IL), especially IL-1 and IL-6, released by macrophages and lymphocytes, are the primary agents which cause induction of release of these acute phase proteins [6]. Most CRP is produced from liver apart from vascular endothelium in response to interleukin-6 produced from macrophages and adipocytes [16, 17].

Immune activation has been demonstrated to be a significant contributor to HIV disease progression in multiple studies [18, 19, 20 and 21]. It was observed that this immune activation was associated with increased levels of bacterial components in blood. Due to increased microbial translocation from the gastrointestinal tract of patients and this microbial translocation was contributed for HIV diseases progression [22, 23]. Naturally CRP being an acute phase reactant should increase in patients with HIV disease progression and immune activation.

Measuring the alterations in APRs can be a useful clinical marker when an infection or inflammatory response is suspected. Serum levels of reactants like fibrinogen and complement proteins increase as part of the inflammatory response. In patients at the stage of AIDS, the cytokines activating coagulation system is produced leading to increase in fibrinogen serum levels. Our findings were also supported by Hooper WC et.al.[24], Bergamini A et.al. [25], Lijfering WM et.al [26].

Significantly decreased levels of total proteins and albumin were found in HIV positive patients, mainly due to malnutrition, malabsorption, impaired protein synthesis, protein losses, inadequate nutrient intake or absorption, metabolic

alteration, hypermetabolism, or a combination of these; alteration of the gastrointestinal tract; and drug nutrient interactions. Nutritional disorders are often present in HIV/AIDS patients. Early studies showed that weight loss and protein depletion associated with body cell mass depletion [27]. The serum albumin levels were decreased and the serum globulin levels were increased in HIV positive patient. The A/G ratio was found to be reversed in HIV positive patients. Globulins play an important role in maintaining the oncotic pressure in low albumin states in these patients.

We concluded that HIV positive patients with serum albumin lower than 3 gm% generally have a poor prognosis; hence the serum albumin level can be used as a prognostic indicator. These depressed albumin levels could reflect the poor nutritional status, catabolic state of chronic disease evidenced by significant weight loss. C-reactive protein (CRP) concentrations increase markedly with acute invasive infections which parallel the severity of inflammation or tissue injury. This advantage makes CRP a useful marker for the presence of disease, response to therapy, and ultimate recovery. Improved methods of quantifying CRP have led to increased application to clinical medicine.

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