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Biochemical Parameters in Human Immunodeficiency Virus Disease Progression

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Abstract

Human Immunodeficiency Virus (HIV) infection, with the complexity of disease and its progression has become a challenge to human beings. HIV infection leads to variable disease course in different people, amongst them are long term non-progressors, who survive more than 10 years after getting infected. Due to the chronicity of the disease and the extent of morbidity it causes, management of such individuals has become a challenge for physicians treating HIV infected patients. Traditionally HIV disease progression is monitored using TCD4+ cell counts and HIV/RNA viral load. Resource poor countries which cannot afford such expenses are looking forward to tests that can be done easily and are cost effective to monitor HIV disease progression and treatment response. We therefore evaluated certain biochemical parameters in both HIV seropositive treatment naive and those on HAART. Significant differences are observed in the plasma concentration of CK-MB ($p<0.01$), AST ($p<0.05$), LDH ($p<0.01$), Total Cholesterol: HDL ratio were ($p<0.001$), HDL:LDL ratio ($p<0.001$), A/G ratio ($p<0.001$), ALT ($p<0.02$), Serum Albumin ($p<0.001$), and Serum Globulin ($p<0.001$) levels. Serum albumin ($r = -0.191$), Albumin:Globulin ratio ($r= -0.162$), Total protein ($r= -0.029$), LDH ($r= -0.264$), CK/MB ($r= -0.027$), HDL ($r= -0.0380$ and LDL:HDL ratio ($r= -0.032$) were found negatively correlating with TCD4+ cell counts in HIV seropositive patients who are antiretroviral therapy naive. A paired t test of various parameters before and after HAART showed significant results with TCD4+ cells ($p <0.0001$), CK/MB ($p= 0.0451$) and LDL:HDL ratio ($p=0.0341$). The results reemphasize the significance of evaluating certain biochemical parameters in HIV seropositive individuals and their usefulness in the management of disease progression and treatment response.

Introduction

Human Immunodeficiency Virus (HIV) infection, with the complexity of disease and its progression has become a challenge to human beings. A UNAIDS global estimate reveals that currently 33.2 million people are living with HIV infection worldwide [1]. The good news is that incidence of HIV infection showed a steady decline throughout the world. Unavailability of an approved vaccine makes this disease a tough nut to crack. HIV infection leads to variable disease course in different people, amongst them are long term non-progressors, who survive more than 10 years after getting infected [2]. Owing to the chronicity of the disease and the extent of morbidity it causes, management of such individuals has become a challenge for physicians treating HIV infected patients. With the advent of Highly Active Antiretroviral Therapy (HAART), the quality of HIV seropositive patients improved to a greater extent, simultaneously their morbidity and mortality has reduced significantly. Conversely previous research reports have pointed out the effects of HAART on the patients as well as stressed the need to evaluate various hematological parameters before initiating HAART therapy [3,4]. Studies conducted in the past have also demonstrated the role of HIV infection by itself irrespective of HAART therapy can result in the development of metabolic disorders including altered lipid metabolism [5]. Previous reports have also suggested the association of cardiovascular disease (CAD) and HAART therapy [6]. Monitoring the disease progression and the response to HAART is traditionally carried out using TCD4+ cell counts and HIV/RNA viral load. The fact that it is the poor, developing and economically weak third world countries that carry most of the burden of HIV seropositive patients, it becomes financially overburdened to acquire resources and infrastructure necessary for patient management. Considering the above said factors research is now being conducted to find some cost effective, easily performed and freely available surrogate or alternate markers that can help in assessing the HIV disease progression. In the present study we have evaluated certain biochemical parameters in HIV seropositive patients including both who are antiretroviral therapy naive and those on HAART.

Materials and Methods

The study was carried out between June 2009 to May 2010, which included 36 HIV seropositive and antiretroviral therapy naive individuals and 21 HIV seropositive patients presently on HAART since 3-4 months attending Integrated Counseling and Testing Centre (ICTC) situated at Area hospital Siddipet were enrolled in the study. A total of 25 Normal healthy individuals are included in the study as controls. All the subjects included in the study were provided with a Proforma with details of the study and an informed and written consent was obtained. Blood samples were collected following standard laboratory procedures and stored under -20˚C. Their HIV status was confirmed following NACO guidelines using three different ELISA methods [7]. The TCD4+ cell counts were evaluated using Flow Cytometry. Serum Albumin, Globulin, and Albumin:Globulin ratio,

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Serum Glutamate Oxaloacetate Transaminase (SGOT), Total protein, Total cholesterol, High density Lipoproteins (HDL), Low density Lipoprotein (LDL), Lactate Dehydrogenase (LDH) and Creatine Kinase (CK/MB) were evaluated by using Diasys kits in an automatic analyzer.

Results

The results revealed a significant variation in all the parameters among the HIV seropositive patients who are antiretroviral therapy naïve when compared with normal healthy individuals. The TCD4+ cell counts and biochemical parameters showed a slight difference among the HIV seropositive patients who were HAART naïve and those on HAART as shown in (Table 1). Serum albumin, Albumin**:** Globulin ratio, Total protein, LDH, CK/MB, HDL and LDL**:** HDL ratio were found negatively correlating with TCD4+ cell counts in HIV seropositive patients who were antiretroviral therapy naïve. Only SGOT, CK/MB and HDL**:** LDL ratio negatively correlated in those who were on antiretroviral therapy as shown in (Table 2). A pared t test of all the parameter showed statistically significant results with TCD4+ cell counts, Albumin**:** Globulin ratio, LDH, HDL, total Cholesterol, CK/MB, LDL and HDL**:** LDL ratio as shown in (Table 3).

Discussion

Over the time the profile of HIV epidemic has evolved from a life threatening to chronic disease, with the availability of better drugs and thanks to some efficacious resource delivery modalities involving communities and people living with HIV infection. A revolutionary new approach in the treatment endorsed by UNAIDS and WHO, simplified HIV diagnostic technologies and gave hope for achieving universal access to prevention, care and treatment of HIV/AIDS even in resource constrained settings. This resulted in prolonging survival and quality of care for people living with HIV/AIDS. The study results show a clear picture of altered biochemical parameters in HIV seropositive patients as observed in previous report by AC Ene et al. [8] in Nigeria. The study results also confirms a recent research published by Suraya Rasheed in USA showing the involvement of HIV infection alone and with no influence of HAART can deregulate the metabolic pathways [9]. Serum albumin, Globulin, Albumin: Globulin ratio and Total protein were found to be statistically significant in HIV seropositive and HAART naive patients as observed in previous studies [10,11]. This observation agrees with previous study that suggested evaluation of these parameters in HIV seropositive patients before initiation of HAART therapy and regularly followed up to assess the treatment response [3]. The serum SGOT, CK/MB, LDH, Total cholesterol, Total cholesterol **:** HDL ratio, LDL, LDL**:**HDL ratio were elevated after the HAART therapy as evidenced in previous studies indicating the possible development of Cardiovascular disease (CAD) due to antiretroviral therapy [12,13]. In the event of global HIV prevalence the bulk of HIV infected individuals is carried by the sub Saharan Africa and the

Parameter	Normal controls Mean ± SD (n=25)	HAART - Mean ± SD (n=36)	p value	HAART+ Mean ± SD (n=21)	p value	p value before and after HAART
CD4+ Tcells		382.08±124.71		78.38±21.99		<0.0001
Serum Albumin	3.72±0.53	4.43±1.03	=0.0025*	4.38±0.64	=0.0004*	<0.0001
Serum Globulin	3.1±0.43	3.28±1.37	=0.5284	3.25±1.05	=0.5171	<0.0001
Albumin:Globulin	1.12±0.19	1.68±0.98	=0.0076*	1.51±0.72	=0.0124*	<0.0001
Tot. Protein	6.82±0.74	7.62±1.16	=0.0035*	7.60±0.90	=0.0024*	<0.0001
SGOT	23.28±9.57	38.33±35.32	=0.0425*	37±25.20	=0.0155*	<0.0001
LDH	339.04±48.50	220.42±79.04	<0.0001*	188.76±42.91	<0.0001*	<0.0001
CK/MB	15.64±4.59	18.06±9.52	=0.2457	15.38±7.34	=0.8842	<0.0001
Cholesterol	161.12±23.12	136.08±27.27	=0.0004*	133.33±21.72	=0.0001*	<0.0001
HDL	48.76±12.30	45.89±7.05	=0.2509	44.05±8.44	=0.1448	<0.0001
Cholest:HDL	3.44±0.85	3.04±0.60	=0.0351*	3.08±0.58	=0.1072	<0.0001
LDL	103.12±14.38	157.42±36.03	<0.0001*	175.43±24.42	<0.0001*	<0.0001
LDL:HDL	2.21±0.55	3.48±0.94	<0.0001*	4.11±0.99	<0.0001*	<0.0001

*Statistically significant

Table 1: The mean, Standard deviation , p value in Normal controls , HAART naive and HAART receiving HIV seropositive patients.

Parameter	HAART - r value	HAART- p value	HAART+ r value	HAART+ p value
CD4+ Tcells		<0.0001		<0.0001
Serum Albumin	-0.191	<0.0001	0.227	<0.0001
Serum Globulin	0.055	<0.0001	0.093	<0.0001
Albumin:Globulin	-0.162	<0.0001	0.194	<0.0001
Tot. Protein	-0.029	<0.0001	0.237	<0.0001
SGOT	0.074	<0.0001	-0.104	<0.0001
LDH	-0.264	<0.0001	0.568	<0.0001
CK/MB	-0.027	<0.0001	-0.084	<0.0001
Cholesterol	0.147	<0.0001	0.451	<0.0001
HDL	-0.038	<0.0001	0.345	<0.0001
Cholest:HDL	0.125	<0.0001	0.056	<0.0001
LDL	-0.032	<0.0001	0.217	<0.0001
HDL:LDL	0.031	<0.0001	-0.086	<0.0001

Table 2: The Correlation coefficient(r value) and unpaired t test (p value) of various parameters in relation to CD4+ Tcells in both HAART naïve and HAART receiving HIV seropositive patients.

Parameter	Paired t test
CD4+ Tcells	<0.0001*
Serum Albumin	=0.9605
Serum Globulin	=0.9176
Albumin:Globulin	=0.4386
Tot. Protein	=0.8640
SGOT	=0.6106
LDH	=0.2388
CK/MB	=0.0451*
Cholesterol	=0.2485
HDL	=0.3623
Cholest:HDL	=0.8872
LDL	=0.0867*
HDL:LDL	=0.0341*

*Statistically significant

Table 3: Paired t test of all the parameters before and after receiving HAART.

Indian subcontinent. The availability and affordability of HAART has dramatically reduced the mortality of HIV infected people and increased the life expectancy. The poor financial position of some third world countries makes it difficult to manage the HIV infected patients which requires costly Infrastructure to assess regularly the TCD4+ cell counts and HIV/RNA viral load. In such cases the patient management can be done and disease progression assessed by other surrogate or alternate markers which show promise as observed in the current as well as recent studies. The present study results indicate effectiveness of serum albumin, globulin, Albumin**:** Globulin ratio in predicting the disease stage or monitoring the disease progression in HIV infected and antiretroviral therapy naive patients. The cardiovascular profile including the serum SGOT, CK/MB, LDH, Total cholesterol, Total cholesterol**:** HDL ratio, LDL, and LDL**:** HDL ratio can be beneficial in assessing the disease progression and treatment response in HIV infected patients who were on HAART therapy. In conclusion we recommend that the Management of HIV/AIDS in the HAART era should include focusing on using our resources as effectively and efficiently as possible to maximize the benefit. The spectrum of HIV care needs to evolve in to a comprehensive primary care model that has an integrated, patient centered approach, and should be linked to specialist care where and when needed.

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