

## Research Article

# Study of serum albumin as surrogate marker of immune suppression in patients living with HIV and AIDS

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## ABSTRACT

**Background:** HIV/AIDS being a life long illness requires regular monitoring. CD<sub>4</sub><sup>+</sup> cell counts and HIV RNA levels have been widely accepted as the most reliable indicators of HIV disease progression but these tests are not readily available and costly too. This study examines that whether Serum albumin levels can be used as a surrogate marker for HIV disease monitoring as an alternate to CD<sub>4</sub> cell count and HIV viral load measurements in low resource set-up. **Methods:** This prospective observational study was conducted at a tertiary care hospital in Central India. We studied a total of 100 PLHIV (patients living with HIV and AIDS). Correlation of CD<sub>4</sub> count was done with serum albumin levels at baseline and at follow-up visits.

**Results:** Several studies have suggested that albumin could serve as a useful marker of HIV disease progression in resource-limited settings. In the present study, the baseline and follow up values of albumin and CD<sub>4</sub> counts were obtained. It was found to have a strong positive correlation amongst them with low CD<sub>4</sub> cell counts being associated with lower serum albumin concentrations.

**Conclusions:** The results of this study suggest that serum albumin levels have potential to be used as a surrogate low-cost prognostic marker for HIV disease monitoring in resource-limited settings where frequent estimation of CD<sub>4</sub> cell count and HIV viral load is not possible.

**Keywords:** HIV, Serum albumin, CD<sub>4</sub> cell

## INTRODUCTION

HIV/AIDS being a life long illness, requires regular monitoring and treatment that is guided by clinical, immunological and viral status of patients living with HIV and AIDS (PLHIV).<sup>1</sup> The disease progression in HIV is defined on the basis of clinical features, CD<sub>4</sub> cell count and HIV virus levels estimated by RNA or DNA PCR.<sup>2</sup> CD<sub>4</sub><sup>+</sup> cell counts and HIV RNA levels have been widely accepted as the most reliable indicators of HIV disease progression. RNA levels are more sensitive and define earlier deterioration or improvement in patients but the onset of various opportunistic infections cannot be

correlated with the viral load. Therefore, CD<sub>4</sub> count has been used generally in defining stages of illness in HIV.<sup>3,4</sup> CD<sub>4</sub> cell count and HIV viral load measurements are readily available and widely utilized in developed world, but same is not the case with the developing countries where, demographic, financial, logistical and technical issues limit the use of CD<sub>4</sub> count and Viral RNA levels. As an alternate to these two tests, many other biological and biochemical markers have been tried to prognosticate or qualitatively define various stages of HIV disease. Many alternatives have been tried as alternate and a few candidates have shown some promise in different studies like lymphocyte count, serum albumin

level, serum albumin/globulin ratio, CRP, DHEAS, serum IgA,  $\beta_2$  microglobulin, p24 antigen,  $CD_8^+$  cell counts, level of  $CD_{38}$  On  $CD_8^+$  cells, platelet counts etc.<sup>5</sup> Baseline serum albumin level in cases with  $CD_4$  count <200 has been associated with increased mortality.<sup>6</sup>

Albumin is the most abundant protein in human body. It is produced in liver and has a half-life of approximately 21 days. Low serum albumin is recognized as an indicator of poor nutritional status, and it has been found to be associated with higher rates of mortality in various acute and chronic conditions.<sup>7</sup> Serum albumin has been studied in HIV/AIDS cases by various researchers and few studies show that the levels of albumin are related to disease progression in HIV irrespective of nutritional status.<sup>8</sup> Recent studies have also suggested that low levels of serum albumin are associated with disease progression, AIDS associated mortality and all-cause mortality in PLHIV independent of  $CD_4$  cell Counts and HIV RNA titre.<sup>8</sup> Serum albumin level could be useful, cheap and easily available surrogate test for predicting severity of HIV infection, for pretreatment assessment & clinical monitoring of response to anti retro viral therapy and as a predictor of survival.<sup>6</sup>

## METHODS

This prospective observational study was conducted at ART center on M.Y. HOSPITAL during the period of October 2013 to March 2014. One hundred consecutive adult HIV/AIDS patients were enrolled after taking informed consent. Patients with pre-existing liver dysfunction, renal dysfunction, or gastrointestinal disease causing decrease in albumin level and patients with clinical evidence of congestive cardiac failure, shock or with history of burns in last 21 days were not included in study. Patients of age less than 18 years, pregnant females and prisoners were excluded from study. Prior approval from institutional scientific review board and the institutional ethic committee was obtained for conducting the study.

All patients were subjected to a detailed history, clinical examination and laboratory investigations including hemoglobin, total and differential WBC counts, liver function tests with serum albumin level, renal function tests,  $CD_4^+$  cell counts and urine examination. Patients were called for follow up after 6 month and serum albumin level,  $CD_4^+$  cell count, hemoglobin and total and differential WBC counts were repeated.

## RESULTS

In our study group, mean age was  $39.6 \pm 10.7$  years. The ages of youngest patient of 20 years age and oldest being 64 years of age. Maximum 38% cases were between 31-40 years of age (Table 1).

Kuppuswami class profile of all cases was performed and it showed that most of the studied patients (46%) were in

socioeconomic class 2, 28% patients were in socioeconomic class 3 while 18% patients were of socioeconomic class 4. Kuppuwami class 5 patients were least in number (5%) (Table 2).

**Table 1: Age distribution.**

Age (in years)	No of patients		Percentage
	Male (N=72)	Female (N=28)	
18-20	01	0	01%
21-30	12	09	21%
31-40	29	09	38%
41-50	12	08	20%
51-60	16	02	18%
61-70	02	0	02%

**Table 2: Socioeconomic class.**

Class	Male	Female	Percentage
1	0	0	0%
2	34	12	46%
3	22	06	28%
4	08	10	18%
5	08	00	08%

In present study, most of the patients were diagnosed with HIV/AIDS for more than 1 year (42%), while 28% were diagnosed between 6 to 12 months and 12 % patients were diagnosed in last 3 months (Table 3).

**Table 3: Duration of illness.**

Duration (since diagnosed)	Male	Female	Percentage
<3 months	10	2	12%
3-6 months	16	2	18%
6-12 months	18	10	28%
>1 year	28	14	42%

In our study, 54% patients had one or more opportunistic infections during the study period of which the most common was oral candidiasis (24) followed by extra pulmonary tuberculosis (12%). Other common opportunistic infections were herpes zoster (12%), pulmonary tuberculosis and Cryptococcal meningitis (Table 4).

In our study, most common presenting complaint of patients was fever (26%) followed by cough (18%), diarrhea (12%) and neck swelling (10%). Other common presentation was skin lesions, seizures and weight loss. 4% patients were found positive during routine pre-operative screening. Breathlessness as the presenting symptom was seen in only 2% of the cases (Table 5).

**Table 4: Opportunistic infection.**

Types of infection	Male	Female
Oral candidiasis	18	6
Herpes zoster	10	2
Pulmonary TB	6	0
Extra pulmonary TB	12	0
Cryptococcal meningitis	2	0

**Table 5: Clinical presentation.**

Clinical Presentation	Percentage
Fever	26%
Cough (productive)	10%
Cough (non-productive)	08%
Diarrhoea	12%
Seizure	08%
Altered sensorium	02%
Weight loss	08%
Neck swelling	10%
Breathlessness	02%
Preoperative check up	04%
Skin lesion	10%

In our study at baseline 50% patients had CD<sub>4</sub> counts <200/ $\mu$ L, 40% patients were having CD<sub>4</sub> counts 200-500/ $\mu$ L and 10% patients had CD<sub>4</sub> counts >500. At the

end of the 6 month observation period 44% patients had CD<sub>4</sub> counts <200/ $\mu$ L, 45 % patients had CD<sub>4</sub> counts 200-500/ $\mu$ L while 11% patients had CD<sub>4</sub> counts >500/ $\mu$ L (Table 6).

**Table 6: Distribution of patients at different CD<sub>4</sub> cells counts level.**

CD4 counts (/ $\mu$ L)	Baseline	At 6 months
<200	50	44
200-500	40	45
>500	10	11

In our study at baseline, of the total 50 patients having CD<sub>4</sub> counts <200/ $\mu$ L, 03 patients were having serum albumin level between 1.5-2.0 gm/dl, 12 patients had albumin level between 2.1-2.5 gm/dl meanwhile 27 patients had serum albumin level between 2.6-3.0 gm/dl and 08 patients had Serum Albumin level between 3.1-3.5 gm/dl.

At the end of 6 months, total 44 patients had CD<sub>4</sub> counts <200/  $\mu$ L. Of these 44 patients, 09 patients had serum albumin level between 1.5-2.0 gm/dl, 05 patients had Serum Albumin level between 2.1-2.5 gm/dl, 24 patients between 2.6-3.0 gm/dl and 06 patients had Serum Albumin level between 3.1-3.5 gm/dl (Table 7,8).

**Table 7: S. albumin & CD<sub>4</sub> cell counts correlation.**

CD <sub>4</sub> cells counts	1.		2.		3.	
	CD <sub>4</sub> $\uparrow$	Serum albumin $\uparrow$	CD <sub>4</sub> $\downarrow$	Serum albumin $\downarrow$	CD <sub>4</sub> ( $\uparrow/\downarrow$ )	Serum albumin( $\downarrow/\uparrow$ )
<200		29		13		08
200-500		10		22		08
>500		0		07		03

**Table 08: Serum albumin at different CD<sub>4</sub> counts.**

CD <sub>4</sub> Counts	<200/ $\mu$ L		200-500/ $\mu$ L		>500/ $\mu$ L	
	Baseline	At 6 months	Baseline	At 6 months	Baseline	At 6 months
1.5-2.0	03	09	02	0		
2.1-2.5	12	05	02	02		
2.6-3.0	27	24	11	18	02	0
3.1-3.5	08	06	22	19	04	0
3.6-4.0			03	05	04	11

## DISCUSSION

In our study total number of cases was 100. 28% of the patients were females and 72% were males. The study of S Shah et al<sup>9</sup> showed similar pattern of presentation. In a similar study by Manish Ghate et al<sup>10</sup> the number of females was 16% and males 84%. The gross difference in

presentation of males and females is due to multiple factors like. Males are migrators and primary disease spreaders. It can due to fact that females generally have poor health seeking behavior. It can also be confounding bias due to limited number of patients in the current study.

To assess the impact of socioeconomic structure in the epidemiological presentation, assessment of socioeconomic class was done according to the Kuppaswami Class profile. Most of the studied patients (46 %) were in socioeconomic class 2. None of the other related studies had described a socioeconomic profile. So comparison was not possible.

Most of the patients who presented with HIV/AIDS had duration of illness more than 1 year (42%). This is expected due to the fact that HIV is a chronic illness and improved survival rate is achieved with good antiretroviral drugs provided free of cost at ART centers.

In our study, 54% of the patients were diagnosed to have one or more opportunistic infections during the study period. Oral candidiasis (24%) was the most common opportunistic infection affecting the subjects in our study followed by tuberculosis (20%) (Extrapulmonary-12% and Pulmonary-8%). Manish Ghete et al.<sup>10</sup> reported incidence of OI to be 35.7/100 person years and the most common infection in his study was Tuberculosis. Tuberculosis and oral candidiasis are the most commonly reported HIV-related OI in India.<sup>11</sup>

In our study, most common presenting complaint of patients was Fever (26%) followed by cough (18%), diarrhoea (12%) and neck swelling (10%). In the study of Idindili Boniphace et al.,<sup>12</sup> the majority of the patients presented with clinical features of weight loss (and wasting); chronic cough; and persistent fever for more than 2 weeks. In our study only 2% patients were diagnosed positive during routine testing prior to surgery. This suggests that despite the change in overall disease spectrum in patients due to ART, the presentation of the illness is still the same. This also shows that much work is required in public health programs to improve patient and physician awareness so that more people can be detected in asymptomatic stages. Delayed diagnosis of illness increases chances of poor response to therapy as well.

Maximum number of patients in the study had baseline CD<sub>4</sub> counts of less than 200/ $\mu$ l, indicating that the patients had a very high risk of developing AIDS-defining illness. The study of K. Suresh Babu,<sup>13</sup> the baseline CD<sub>4</sub> count of both the genders was less than 250/ $\mu$ l. It is the reality in most rural, poor communities, like that of ours, that the patients accept a HIV test after suffering for a long time and tried on all kinds of remedies without success. During this time their CD<sub>4</sub> cell counts progressively declined. Most of the patients studied were diagnosed with HIV since 1 year; this also suggests a strong need of re-evaluation of the HIV treatment strategy so that more patients can get benefit of antiretroviral therapy at early stages.

In our study, CD<sub>4</sub> counts and serum albumin levels at presentation and at 6 months did not show any significant improvement but a significant correlation was found

between pre-treatment serum albumin levels and pre-treatment CD<sub>4</sub> cell count pre-treatment serum albumin levels and pre-treatment weight. Analysis of change in CD<sub>4</sub> counts with change in serum albumin level showed significant positive association with correlation coefficient of 0.52 (baseline) and 0.51 (follow up) with both statistically significant p values of <0.001. This is in agreement with the study of Olawuni HO et al.<sup>14</sup> Albumin is also called as negative phase reactant and is been seen in association with some other chronic illnesses like tuberculosis. Also in our study, falling albumin level correlated with disease progression.<sup>15</sup>

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