



ROLE OF SERUM ALBUMIN LEVEL COMPARED TO CD4+ CELL COUNT AS A MARKER OF IMMUNOSUPPRESSION IN HIV/AIDS PATIENTS

Medicine

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ABSTRACT

Background and Objectives: - CD4+cell counts and HIV RNA levels are prognostic indicators of HIV disease progression but in developing countries their use is limited due to cost and technology constraints. So there is a need to identify alternate prognostic markers of immunosuppression. Recent studies have suggested that low levels of serum albumin are associated with rapid disease progression and AIDS associated mortality independent of CD4+ cell counts and HIV RNA titre. This study aims at establishing role of serum albumin level as a surrogate marker in HIV / AIDS patients as compared to CD4+cell counts. Objective of the study is to monitor and follow up the levels of serum albumin and absolute CD4+ cell counts in HIV infected individuals and assess their correlation as a marker of immunosuppression.

Methods: - This prospective follow up case study included 60 HIV/AIDS patients presenting to new hospital government medical college at Kota, Rajasthan during the period of march 2019 to February 2020. Descriptive and Analytical statistics were done to find correlation of albumin with CD4+ t lymphocyte count in HIV/AIDS patients.

Results: - 39.8% cases were between 31-40 years of age and 70% were males. 58.3% of the patients were diagnosed recently in last three months and fever (30%) was most common presenting complaint. Most common opportunistic was pulmonary tuberculosis (38.3%). Albumin showed a direct correlation with CD4 count both at baseline ($p<0.001$) and during follow up ($p<0.001$) in cases. Regression analysis showed linear trend between albumin and CD4 count. ($p=0.01$)

Conclusion: - There was a strong direct correlation between CD4 count and albumin in cases both at baseline and follow up and regression analysis showed significant linear trend indicating that albumin could be used as a surrogate marker for immunosuppression in HIV/AIDS patients.

KEYWORDS

HIV, AIDS, CD4, Albumin, Marker

INTRODUCTION:

Human immunodeficiency virus (HIV) is a lentivirus (a member of the retrovirus family) that causes acquired immunodeficiency syndrome (AIDS), a condition in humans in which progressive failure of the immune system allows life-threatening opportunistic infections and cancers to thrive¹. HIV infection in humans is considered pandemic by the World Health Organization (WHO). HIV infects about 0.6% of the world's population.² In 2009, AIDS claimed an estimated 1.8 million lives, down from a global peak of 2.1 million in 2004. Intensified awareness and preventive measures, as well as the natural course of the epidemic have played a role. Nevertheless an estimated 2.6 million people were newly infected in 2009.³

HIV infects vital cells in the human immune system such as helper T cells (specifically CD4⁺ T cells), macrophages, and dendritic cells. HIV infection leads to low levels of CD4⁺ T cells through three main mechanisms: First, direct viral killing of infected cells; second, increased rates of apoptosis in infected cells; and third, killing of infected CD4⁺ T cells by CD8 cytotoxic lymphocytes that recognize infected cells. When CD4⁺ T cell numbers decline below a critical level, cell-mediated immunity is lost, and the body becomes progressively more susceptible to opportunistic infections.⁴

HIV progresses to AIDS at a variable rate affected by viral, host, and environmental factors; most will progress to AIDS within 10 years of HIV infection. Treatment with anti-retrovirals increases the life expectancy of people infected with HIV. Even after HIV has progressed to diagnosable AIDS, the average survival time with antiretroviral therapy was estimated to be more than 5 years. Without antiretroviral therapy, someone who has AIDS typically dies within a year.⁵

CD4+cell counts and HIV RNA levels have been widely accepted as the most powerful prognostic indicators of HIV disease progression.⁶

Use of these markers is wide spread in developed countries, but in developing countries they are not regularly obtained due to cost and technology constraints. While they remain as main clinical markers, they do not fully explain an individual's prognosis.⁷

There is a need to identify and establish efficacy of alternate prognostic markers of immunosuppression. Following few candidates have been proposed Total Lymphocyte Count, Serum Albumin, Albumin/Globulin Ratio, Haemoglobin, Hematocrit, CRP, DHEAS, , IgA, β 2microglobulin, p24 Antigen, CD8+ Cell Counts, Level Of CD38 On CD8+ Cells, Platelet Counts.⁸

Low levels of serum albumin have been associated with higher rates of mortality in different acute and chronic conditions⁹. Recent studies have suggested that low levels of serum albumin are associated with rapid disease progression to AIDS ,AIDS associated mortality and all cause mortality , independent of CD4 cell counts and HIV RNA titre.¹⁰

Serum Albumin Level could prove to be a very useful, cheap and easily available surrogate test for predicting severity of HIV infection and for pretreatment assessment¹¹ & clinical monitoring of response to anti retro viral therapy¹² and as a predictor of survival.¹³

This study aims at establishing role of Serum Albumin Level as a surrogate marker of immunosuppressed state of HIV infected individuals as compared to CD4+cell counts and assess correlation of albumin and absolute CD4+ cell counts as a marker of immunosuppression.

MATERIALS AND METHODS:

Study population, place and duration: This study was conducted on 60 HIV/AIDS patients presenting to Department of Medicine, with written informed consent, willing for regular follow up, in New Hospital Government Medical College Kota, Rajasthan during the period of March 2019 to February 2020 (1 years). Present study had 42 males (70%) and 18 female subjects (30%).

Study design: Prospective follow-up study

Method of collection of data: A detailed history , clinical examination and laboratory investigations including Haemoglobin, Total And Differential WBC Counts, Hematocrit , Liver Function Tests with Serum Albumin Level , Renal Function Tests, CD4+ Cell Counts, Urinary Albumin & HIV ELISA AND WESTERN BLOT , HIV RNA estimation (wherever possible) and Stool analysis (wherever necessary) was done. Repeat measurements on 6th month follow up include Albumin, CD4+ cell count, Haemoglobin, Total and Differential WBC counts.

INCLUSION CRITERIA: HIV infected/AIDS patients > 18 years of age.

EXCLUSION CRITERIA:

- Any pre-existing hepatobiliary disease causing decrease in albumin level.
- Any pre-existing renal disease / chronic kidney disease causing decrease in albumin level.
- Any pre-existing gastrointestinal disease causing decrease in albumin level.
- Any clinical evidence of congestive cardiac failure
- Any clinical evidence of shock
- Any history of burns in last 21 days

Ethical clearance: Due permission from institutional ethical committee was obtained.

Data analysis:

Data was recorded on a Performa. The data analysis was computer based; SPSS-22 will be used for analysis. For categoric variables chi-square test was used. For continuous variables independent samples's *t*-test will be used. In order to know the association between albumin and cd4 cell count simple (pearson) correlation coefficient was estimated. Positive or negative *r* value indicating positive or negative correlation. *p*-value <0.05 was considered as significant.

RESULTS AND DISCUSSION:

In the present study, the relationship between serum albumin and absolute CD4+ cell count was studied in 60 HIV/AIDS patients who presented to Govt Medical College Kota, Rajasthan during the period between March 2019 To February 2020. Apart from descriptive analysis, correlation of CD4 count was done with serum albumin levels. Follow up was done in all 60 cases and correlation between albumin and CD4 count was done in these cases. (Table 1)

Table 1: Analytical Statistics: Correlation In Cases

Parameters	Statistical tools	cd4 count	albumin	f/u cd4	f/u albumin
cd4 count	Pearson Correlation	1	.512**	1	.520**
	Sig. (1-tailed)	--	.000	--	.000
	Sum of Squares	2076302.583	3402.036	1906277.333	3460.800
	Covariance	35191.569	57.662	32309.785	58.658
albumin	Pearson Correlation	.512**	1	.520**	1
	Sig. (1-tailed)	.000		.000	
	Sum of Squares and Cross-products	3402.036	21.233	3460.800	23.264
	Covariance	57.662	.360	58.658	.394

*Correlation is significant at the 0.01 level (1-tailed) P VALUE < 0.001

Table 2 : Laboratory Parameters

Study parameters	Cases	
	Baseline	Follow-up
Haemoglobin(mg/dl)	11.222.08	11.232.01
Total count(cells/mm ³)	68852565	70382190
Cd4 count(cells/mm ³)	269.5187.5	268.67179.7
Albumin(gm/dl)	3.020.6	3.040.6

The laboratory parameters were studied and showed no significant change in mean haemoglobin, albumin and Cd 4 counts at baseline and third month follow up visit. (Table 2)

Hence sub-analysis was done for cases after categorization of cases into low Cd4 (<200) and other category with count >200

Table 3: Albumin and CD4 levels in cases.

Albumin Levels	CD4 < 200	CD4> 200
Baseline	2.85	3.19
Follow Up	2.84	3.24

Follow up showed a downward trend in the albumin levels in study

patients from baseline levels in the category of patients with initial cd4 counts < 200. This was probably due to the low immune status of these patients and more time required for the stabilization of falling counts before a rising trend is noted.

For patients with cd4 counts > 200 a linear an upward rising trend was present in the level of cd4 count at follow up. (Table 3)

In the study done by Mehta et al¹⁰ the effect of albumin before and after HIV seroconversion on disease progression was examined among individuals already infected with HIV at entry into a community-based cohort (n = 453) and further assessed among HIV seroconverters with albumin concentrations measured after (n = 219) and before seroconversion (n = 138). The prognostic effect of albumin on AIDS, AIDS mortality, and all-cause mortality was examined and among 453 HIV-infected individuals, albumin <35 g/liter was associated with faster progression to AIDS [adjusted relative hazard (ARH), 1.8], AIDS mortality (ARH: 2.2), and all-cause mortality (ARH: 2.4). Analyses restricted to HIV seroconverters were similar. Preseroconversion levels of albumin did not predict outcomes, but HIV seroconversion appeared to lower albumin levels. These data showed that albumin <35 g/liter after HIV seroconversion was associated with faster HIV disease progression and suggested that low albumin levels are probably a consequence of HIV infection rather than merely reflective of some individuals inherently having low albumin levels.¹⁰

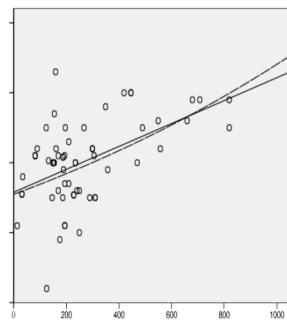
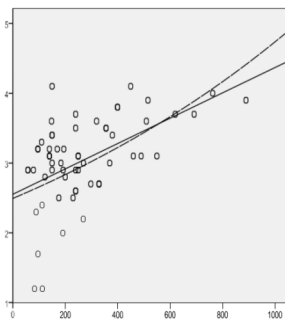
In a study done by Kannangai R et al⁸ at CMC Vellore the usefulness of alternate prognostic serum and plasma markers for antiretroviral therapy for human immunodeficiency virus type 1 infection were studied which included dehydroepiandrosterone sulfate (DHEAS), albumin, and C-reactive protein (CRP). Paired blood samples were collected from patients before and after ART and ATT initiation. Differences in the albumin levels before and after ART or ATT were significant (P < 0.05), while the differences in DHEAS and CRP levels were not significant (P > 0.05).⁸

Shah S et al⁷ did study to describe gender differences in haemoglobin and albumin and to investigate the prognostic value of these measurements in relation to highly active antiretroviral therapy (HAART). In the 495 patients included in this analysis, haemoglobin and albumin levels were both significantly related to short-term risk of AIDS and death independently of CD4 count [hazards ratio (HR)=0.73/g/dL higher haemoglobin, P<0.0001 and HR=0.87/g/L higher albumin, P<0.0001] and prognostic value did not differ by gender.⁷

In the study done by Olawumi and Olatunji¹¹ the possible importance of serum albumin measurement in assessing AIDS stage and in monitoring the response to highly active antiretroviral therapy using CD4 cell count and body weight as parameters was examined in 185 consecutive HIV-infected, therapy-naïve individuals who were recruited for antiretroviral therapy. There were significant positive correlations between pretreatment albumin and both pretreatment CD4 cell count and pretreatment weight, and between post-treatment albumin and both post-treatment weight and post-treatment CD4 cell count up to a count of 700 cells/microL. There were also significant positive correlations between increase in serum albumin and both increase in body weight and duration of treatment.¹¹

In the present study, the baseline and follow up values of albumin and cd4 counts were obtained and it was found to have a strong positive correlation amongst them, with correlation coefficient of 0.52 (baseline) and 0.51 (follow up) with both statistically significant *p* values of < 0.001. This suggests that serum albumin levels can be used as a surrogate marker for HIV disease monitoring as also showed in study by Oluwami.¹¹ Though such strong correlation in short term (6 month) follow up used in this study is an indicator of usefulness of albumin as a surrogate marker but for further assessment of its effect on mortality needs a longer duration of follow up in a bigger study cohort as had been shown before in the study done by Mehta et al.¹⁰

Regression analysis showed significant linear trend suggesting albumin as a variable is an important factor affecting change in Cd4 count (*p*=0.01) (Graph 1 & 2)

albumin**Follow-up albumin****Cd4 count****Follow up Cd4 count**

Graph 1 and 2: Regression Scatter Plot in Cases Baseline And Follow Up

CONCLUSIONS:

There was a strong direct correlation between CD4 count and Albumin in cases both at baseline and follow up indicating that albumin could be used as a surrogate marker for immunosuppression in HIV/AIDS patients.

Conflict of interest: There is no conflict of interest between authors.

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