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

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ABSTRACT Background: Human immunodeficiency virus (HIV) is a lenti virus (a member of the retrovirusfamily) that causes acquired immunodeficiency syndrome (AIDS), a condition inhumans in which progressive failure of the immune system. CD4+cell counts and HIV RNA levels have been widely accepted as the most powerful prognostic indicators of HIV disease progression. Use of these markers is wide spread in developed countries, but in developingcountries they are not regularly obtained due to cost and technology constraints. So there is a need to identify and establish efficacy of alternate prognostic markers of immunosuppression other than CD4+ cell count for HIV. Objectives: To evaluate the role of Serum Albumin Level as a surrogate marker of immunosuppressed state of HIV infected individuals as compared to CD4+cell counts and study direct correlation between albumin level and CD4 count both at baseline and follow-up. Methods: Prospective case control study was conducted on 100 HIV/AIDS patients presenting to presenting to Osmania medical college/ Osmania General Hospital, Hyderabad during the period of November 2013to October 2015. A detailed history,clinical examination and laboratory investigations including Hemoglobin, 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) shall be done. Repeat measurements on 3rd month follow up include Albumin, CD4+ cell count, hemoglobin, and Total and Differential WBC counts Results: In our study 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. (correlation coefficient= 0.54 (p<0.01). Conclusion : Albumin and Albumin/ Globulin ratio could be used as a supplementary marker for immunosuppression in HIV/AIDS patients.

INTRODUCTION

Human immunodeficiency virus (HIV) is a lenti virus (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. AIDS was first recognized in the United States in the summer of 1981[2]

HIV infection in humans is considered pandemic by the World Health Organization (WHO). From its discovery in 1981 to 2006, AIDS killed more than 25 million people. HIV infects about 0.6% of the world's population3. In 2008, the estimated number of new HIV infections was approximately 30% lower than at the epidemic's peak 12 years earlier4. An estimated 2.6 million people were newly infected in 20095. 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 direct viral killing of infected cells, increased rates of apoptosis in infected cells &killing of infected CD4+ T cells by CD8 cytotoxic lymphocytes that recognize infected cells6. Without antiretroviral therapy, someone who has AIDS typically dies within a year7 . CD4+cell counts and HIV RNA levels have been widely accepted as the most powerful prognostic indicators of HIV disease progression8. CD4+cell counts and HIV RNA levels have been widely accepted as the most powerful prognostic indicators of HIV disease progression. Use of these markers is wide spread in developed countries, but in developing countries they are not regularly obtained due to cost and technology constraints9.There is a need to identify and establish efficacy of alternate prognostic markers of immunosuppression which prompted us to do this study.

AIMS AND OBJECTIVES

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+cellcounts. To monitor and follow up the levels of serum albumin and absolute CD4+ cell counts in 100 HIV infected individuals and assess their correlation as a marker of immunosuppression. To study direct correlation between albumin level and CD4 count both at baseline and follow-up.

METHODOLOGY

This is a prospective Follow up Case Control Study conducted at Osmania Medical College and Hospital, Hyderabad on 100 HIV/AIDS patients presenting to our hospital, between November 2013to October 2015. 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) were done. Repeat measurements done on 3rd month follow up included Albumin, CD4+ cell count, hemoglobin, and total and differential WBC count.

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

EXCLUSION CRITERIA

A. Any pre-existing hepatobiliary disease causing decrease in albumin level.

B. Any pre-existing renal disease / chronic kidney disease causing decrease in albumin level.

C. Any pre-existing gastrointestinal disease causing decrease in albumin level.

D. Any clinical evidence of congestive cardiac failure.

E. Any clinical evidence of shock.

F. Any h/o burns in last 21 days.

A complete general and systemic physical examination will be

done in all cases. Peripheral blood will be drawn from all the study subjects under aseptic biosafety precautions Albumin measured in serum (yellow-top tube) AND method used is bromocresol green Olympus AU2700 analyzer. CD4+ T lymphocyte counting will be done in automated four-color BD – two laser FACS calibre with multiset software instrument using flow cytometry single platform technology.

ETHICAL CLEARANCE
Ethical clearance was obtained from Osmania medical college/Osmania general hospital.

STATISTICAL ANALYSIS
The data was tabulated and analyzed. The quantitative data was summarized in excel sheet. Mean, median, standard deviation was estimated .In order to know the association between albumin and cd4 cell count simple (Pearson) correlation coefficient was estimated. A Positive or negative r value indicates positive or negative correlation. In all above tests "p" value less than 0.05 was accepted as indicating statistical significance. SPSS 17 software was used. Microsoft word and excel was used for preparation of graphs and charts.

RESULTS
Total100 HIV/AIDS patients were included in the study. 100 Age and sex matched subjects were selected from normal population as controls, who were HIV negative. Follow up was done in all 100 cases and controls.

Table 1. Distribution of patients based on Age

Parameter	Cases	Controls	P Value
	Mean±SD	Mean±SD	
Age	39.6±10.8	39.74±10.3	0.926

As shown in the table 1 there was no significant difference in the mean ages between cases and controls(P>0.05). There were 31 females and 69 males in both cases and controls.

Most common opportunistic infection was pulmonary tuberculosis. Heterosexual behavior is the most common risk factor of our study patients

Table 2. Laboratory parameters

Parameter	Cases baseline	Cases Follow up	Cases baseline	Cases Follow up
	Mean ± SD	Mean ± SD	Mean ± SD	Mean ± SD
Hemoglobin	11.24 ± 2.08	11.23 ± 2.02	12.29 ± 1.5	12.32 ± 1.45
Total count	6845 ± 2594	7009 ± 2209	7170 ± 2117	7150 ± 1988
CD4 count	273.4 ± 191.2	271.5 ± 182.1	1018.7 ± 241	1020.8 ± 237
Albumin	2.9 ± 0.62	3 ± 0.64	4.02 ± 0.69	3.89 ± 0.6

Comparison of baseline and follow up visit for the above laboratory parameters was done it was observed that there was no significant change in mean hemoglobin, total count, CD4 count and albumin in cases and in controls.

Table 3. Correlations in cases

		CD4	Albumin	Follow up Albumin	Follow up CD4
CD4	Pearson correlation	1	.541**	570**	..980**
	Sig. (2 tailed)		.000	.000	.000
	N	100	100	100	100
Albumin	Pearson correlation	.541**	1	.737**	.558**
	Sig. (2 tailed)	.000		.000	.000
	N	100	100	100	100
Follow up Albumin	Pearson correlation	.570**	.737**	1	.592**
	Sig. (2 tailed)	.000	.000		.000
	N	100	100	100	100
Follow up CD4	Pearson correlation	.980**	.558**	.592**	1
	Sig. (2 tailed)	.000	.000	.000	
	N	100	100	100	100

**. Correlation is significant at the 0.01 level (2-tailed).

Pearson correlation was done for CD4, follow up CD4 counts, albumin and follow up albumin. It was observed that there was a significantly positive correlation observed between CD4 count and albumin r = 0.541, between CD4 count and follow up albumin r = 0.57, between follow-up CD4 count and baseline albumin r = 0.737 and between follow-up CD 4 count and follow up albumin r = 0.592.

Table 4. Correlations in controls

		CD4	Albumin	Follow up Albumin	Follow up CD4
CD4	Pearson correlation	1	.541**	570**	..980**
	Sig. (2 tailed)		.123	.000	.533
	N	100	100	100	100
Albumin	Pearson correlation	.155	1	.145	.012
	Sig. (2 tailed)	.123		.149	.902
	N	100	100	100	100
Follow up CD4	Pearson correlation	.995**	.145	1	-.074
	Sig. (2 tailed)	.000	.149		.461
	N	100	100	100	100
Follow up Albumin	Pearson correlation	-.063	-.012	-.074	1

	Sig. (2 tailed)	.533	.902	.461	
	N	100	100	100	100
**. Correlation is significant at the 0.01 level (2-tailed).					

In the present study there was no correlation observed in cd4 count and albumin or follow up CD 4 count and follow up albumin with in controls. P>0.05.

DISCUSSION

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 relationship between serum albumin and absolute CD4+ cell count was studied in 100 HIV/AIDS patients who presented to the Osmania medical college / Osmania General Hospital Afzalgunj, Hyderabad during the period between November 2013 to October 2015. Apart from descriptive analysis, correlation of CD4 count was done with serum albumin levels. Follow up was done in all 100 cases and correlation between albumin and CD4 count was done in these cases.

Mean age of patients in this study was39.6 years with SD of 10.8 years in cases and 39.74 + 10.3 in controls. This is similar in comparison to other studies by Shah et al9 , Kannangai et al10. Mehta et al11 Oluwami et al12.

Present study had 69 males (69.0%) and 31 female subjects (31.0%) which was comparable to other studies.

Comparison of baseline and follow up visit for the laboratory parameters was done. It was observed that there was no significant change in mean hemoglobin, total count, CD4 count and albumin in cases and in controls. 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. The other studies had not used a control group for baseline determination of parameters in age and sex matched population. In the study done by Mehta et al9 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 levels9 .

In a study done by Feldman and Joseph G et al on serum albumin as a powerful predictor of survival among HIV-1 infected women, a prospective cohort study of 1941 women enrolled at six sites in the women's interagency HIV study, albumin fell 0.44g/L/y in 1627 women who survived and at a faster rate in 397 who died (1.54 g/L/y; p<0.01). In a time-dependent model adjusting for disease markers, the relative hazard (RH) was fivefold higher in patients with serum albumin <35g/L compared with patients with serum albumin >42 g/L. The RH (relative hazard) of serum albumin <35g/L in women with CD4+ lymphocyte count >=200 cells /[mu]L was 8.2 [95% CI: 4.2-15.8]) versus only 3.8 [95% CI 2.4-6.1] in those with counts <200 cells/mm3. In a fixed covariate Cox analysis of patients who started HAART during the study, albumin prior to HAART was associated with a higher RH (7.0 for albumin <35g/L versus >42 g/L) showing a significant correlation of serum albumin as a strong independent predictor of mortality in HIV-1 infected women13.

CONCLUSIONS

Males were more commonly affected. Most common opportunistic infection was pulmonary tuberculosis. Heterosexual behaviour was the most common risk factor of our study patients. 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(correlation coefficient= 0.54 (p<0.01). Regression analysis showed significant linear trend suggesting albumin as an important variable reflecting change in CD4 count (p=0.01).

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