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

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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 thrive.

AIDS was first recognized in the United States in the summer of 1981, when the U.S. Centers for Disease Control and Prevention (CDC) reported the unexplained occurrence of Pneumocystis jiroveci (formerly P. carinii) pneumonia in five previously healthy homosexual men in Los Angeles and of Kaposi's sarcoma (KS) with or without P. jiroveci pneumonia in 26 previously healthy homosexual men in New York and Los Angeles(1). HIV infection in humans is considered pandemic by the World Health Organization (WHO). The number of people living with HIV/AIDS has been steadily increasing across the world and reached 388 lakh (ranging between 376-404 lakh) in 2015. Global HIV incidence reached its peak in 1997, at 3·3 million new infections (95% uncertainty interval [UI] 3·1-3·4 million). Annual incidence has stayed relatively constant at about 2·6 million per year (range 2·5-2·8 million) since 2005, after a period of fast decline between 1997 and 2005. At the same time, HIV/AIDS mortality has been declining at a steady pace, from a peak of 1·8 million deaths (95% UI 1·7-1·9 million) in 2005, to 1·2 million deaths (1·1-1·3 million) in 2015 (2). 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

HIV associated mortality independent of CD4+ cell counts and HIV RNA titer. 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 titer. 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: 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 100 HIV/AIDS patients with duration of study being 18 months. Descriptive and Analytical Statistics were done to find correlation of albumin with CD4+ T lymphocyte count in HIV/AIDS patients.

Results: Age distribution showed maximum number of cases between 31-40 years of age and 41 – 50 years (32%). Males constituted 54% of cases while females constituted 46% of cases. Study subjects were divided into social classes with most common being class 4 (upper lower)(55%). Most common presenting complaint of patients in this study was fever (35%) and followed by presenting complaint of patients in this study was fever (35%)

Conclusion: There was a strong direct correlation between CD4 count and albumin in both study groups. Such correlation was absent in the controls both at baseline and follow up. Regression analysis showed significant linear trend indicating that albumin could be used as a surrogate marker for immunosuppression in HIV/AIDS patients.

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ABSTRACT

Background: 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. Therefore, 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 titer. This study aims at establishing the role of serum albumin level as a surrogate marker in HIV/AIDS patients.

Methods: This prospective follow-up case study included 100 HIV/AIDS patients with duration of study being 18 months. Descriptive and Analytical Statistics were done to find correlation of albumin with CD4+ T lymphocyte count in HIV/AIDS patients.

Results: Age distribution showed maximum number of cases between 31-40 years of age and 41 – 50 years (32%). Males constituted 54% of cases while females constituted 46% of cases. Study subjects were divided into social classes with most common being class 4 (upper lower)(55%). Most common presenting complaint of patients in this study was fever (35%). Albumin showed a direct correlation with CD4 count both at baseline (p<0.001) and during follow up (p<0.001) in cases. Such correlation was absent in the controls both at baseline and follow up. 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 both study groups. Such correlation was absent in the controls both at baseline and follow up and the regression analysis showed significant linear trend indicating that albumin could be used as a surrogate marker for immunosuppression in HIV/AIDS patients.

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Research Article

At the same time, HIV/AIDS mortality has been declining at a steady pace, from a peak of 1·8 million deaths (95% UI 1·7-1·9 million) in 2005, to 1·2 million deaths (1·1-1·3 million) in 2015 (2). 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. (3) 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 antiretrovirals 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 (4).

**Need for the study**

CD4+ cell counts and HIV RNA levels are prognostic indicators of HIV disease progression in developing countries their use is limited due to cost and technology constraints and so there is a need to identify alternate prognostic markers of immunosuppression.

Following few candidates have been proposed Total Lymphocyte Count, Serum Albumin, Albumin/Globulin Ratio, Hemoglobin, Hematocrit, CRP, DHEAS, IgA, β2microglobulin, p24 Antigen, CD8+ Cell Counts, Level Of CD38 On CD8+ Cells, Platelet Counts (5)

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 titer (6)

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 assessment & clinical monitoring of response to anti retro viral therapy and as a predictor of survival (7-9)

This study aims at establishing role of serum albumin level as a surrogate marker in HIV / AIDS patients as compared to CD4+cell counts.

**METHODS**

Study will include minimum of 100 HIV/AIDS patients coming to ART centre , Visakhapatnam

**Study Design**

Prospective observational study

Study period - January 2017 to June 2018

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) shall be done. Repeat measurements on 6th month follow up include Albumin, CD4+ cell count, Haemoglobin, Total and Differential WBC counts.

**Statistical Analysis**

Descriptive Statistics: Mean and Standard Deviation for variables; Analytical Statistics: χ² test, Independent Student T Test; Pearson Coefficient: Correlation between albumin and CD4+ cell counts.

**RESULTS AND DISCUSSION**

In the present study, the relationship between serum albumin and absolute CD4+ cell count was studied in 100 HIV/AIDS patients. Present study had 54 males (54%) and 46 female subjects (46%). Age distribution showed maximum number of cases between 31-40 years of age(32%) and 41 – 50 years (32%). Study subjects were divided into social classes with most common being class 4 ( upper lower)( 55%).

Most common presenting complaint of patients in this study was Fever (35%) followed by Cough(19%). Diarrhea and Seizures were next common presenting features at 10% and 9% respectively. Significant weight loss was presenting complaint in 8 patients. Opportunistic infections sen in 52 % of total cases and most common of them was candidiasis (36%), out of which oral candidiasis is the commonest form.

Most common high risk behaviour was heterosexual contact (69%) followed by history of blood transfusion(11%). The laboratory parameters were studied and showed no significant change in mean hemoglobin at baseline and sixth month follow up visit for cases.

**Table 1** Socioeconomic status

| SE CLASS | Frequency | Percent |
|----------|-----------|---------|
| 1        | 100       | 100     |

| Variable | N   | Minimum | Maximum | Mean  | SD    | P-value |
|----------|-----|---------|---------|-------|-------|---------|
| Hb[gm%]  | 100 | 7.2     | 15.5    | 11.30 | 2.10  | 0.77    |
| f/u Hb%  | 100 | 7.0     | 15.5    | 11.27 | 1.98  |         |
| Total count | 100 | 1850.0  | 89000.0 | 7752.40 | 8592.62 | 0.09    |
| f/u TC   | 100 | 11000.0 | 11000.0 | 7136.04 | 2135.57 |         |
| CD4+ Count | 100 | 14.0    | 820.0   | 261.71 | 180.71 | 0.023   |
| F/U CD4 Count | 100 | 58.0    | 890.0   | 268.11 | 180.93 |         |
| Serum albumin | 100 | 1.20    | 4.30    | 3.02  | 0.61  | 0.024   |
| F/U Serum Albumin | 100 | 1.20    | 4.1     | 3.05  | 0.63  |         |

Sub analysis of Sr. Albumin was done after categorization of patients into low cd4 (<200) and other category with count >200, which showed decrease in mean albumin on follow up in category with CD4<200.

**Table 3 Serum albumin levels in relation to CD4 count**

| Albumin Levels | CD4 < 200 | CD4> 200 |
|----------------|-----------|----------|
| Baseline       | 2.87      | 3.17     |
| Follow UP      | 2.82      | 3.25     |

The baseline and follow up values of albumin and cd4 counts were found to have a strong positive correlation amongst them, with correlation coefficient of 0.49[baseline] and
0.5265[follow up] with statistically significant p values of < 0.0001 & <0.00001 respectively

Fig 1 Linear regression analysis of serum albumin and CD4 count - baseline

Fig 2 Linear regression analysis of serum albumin and CD4 count - follow up

Table 4 Correlation between Serum albumin and CD4 count

| Relation          | r-value | P-value     |
|-------------------|---------|-------------|
| CD4 count & Sr. Alb | 0.49    | <0.00001    |
| Follow up CD4 count & Sr. Alb | 0.5265 | <0.00001 |

This suggests that serum albumin levels can be used as a surrogate marker for HIV disease monitoring. 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.

CONCLUSION

1. Males were more common and presentation(56%), with fever being the most common presenting symptom(35% cases)
2. Heterosexual behaviour was seen as the most common risk factor of our study patients
3. 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.

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