Original article:

Role of serum albumin level compared to CD4+ cell count as a marker of immunosuppression in HIV infection

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Abstract

Back ground: HIV infection is global pandemic characterized by profound immunosuppresion.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 serum albumin level andcorrelate between serum albumin levels, CD4+ cell count and other markers of immunosuppression like Albumin/Globulin ratio, hematocrit, and platelet count.

Methods: Cross sectional study was conducted on 200 HIV/AIDS patients presenting to and registered at ART Centre JLN Hospital, Ajmer. A detailed history,clinical examination and laboratory investigations including Hb,TLC,DLC,Hematocrit,LFT withSerum Albumin level,RFT,CD4+Cell Counts,HIV Tridot test was done.

Results: In our study the mean albumin level was 3.21 ± 0.68, There was Significant positive correlation between CD4 count and albumin level.[r]=0.784, P<0.001.Also significant direct correlation between CD4 count and Albumin/ Globulin ratio.P<0.001

Conclusion : Albumin and Albumin/ Globulin ratio could be used as a supplementary marker for immunosuppression in HIV/AIDS patients.

Key words – Immunosupression, Hematocrit, CD4+ cell count.

Introduction

AIDS is one of the most devastating infectious diseases in human history, and its causative agent HIV. Shortly after the first reports of AIDS in the United States in 1981 and the isolation of HIV-1, 2 years later, the disease was discovered to be established in heterosexual populations of various parts of the world.[1,2]

HIV : Human immunodeficiency virus (HIV) infection causes morbidity and mortality worldwide, and the number of HIV-infected patients has increased dramatically in the past decade. HIV infection causes systemic diseasewith many complications beyond acquired immunodeficiency syndrome (AIDS) illnesses that may not yet be recognized.

Advances over the past 20 years in the treatment of HIV infection have led to increased life expectancy; yet adjusted mortality rates remain significantly elevated when compared to non-infected individuals.[3]

AIDS definition

The current CDC classification system for HIV-infected adolescents and adults categorizes persons on the basis of clinical conditions associated with HIV infection and CD4+ T lymphocyte counts. The

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system is based on three ranges of CD4+ T lymphocyte counts and three clinical categories. Using this system, any HIV-infected individual with a CD4+ T cell count of <350/μL has AIDS by definition, regardless of the presence of symptoms or opportunistic diseases.[4]

Once individuals have had a clinical condition in category B, their disease classification cannot be reverted back to category A, even if the condition resolves; the same holds true for category C in relation to category B.Persons with positive HIV serology who have ever had a CD4 lymphocytecount below 350 cells/μL or a CD4 lymphocyte percentage below 14% are considered to have AIDS.[5]

Causative agent

HIV is the etiologic agent of AIDS; it belongs to the family of human retroviruses (Retroviridae) and the subfamily of lentiviruses. The four retroviruses known to cause human disease belong to two distinct groups: the human T lymphotropic viruses (HTLV)-I and HTLV-II, which are transforming retroviruses; and the human immunodeficiency viruses, HIV-1 and HIV-2, which cause cytopathic effects either directly or indirectly. The most common cause of HIV disease throughout the world, is HIV-1, which comprises several subtypes with different geographic distributions.[6]

Markers of Immunosupression

The hallmark of symptomatic HIV infection is immunodeficiencycaused by continuing viral replication. The virus can infect all cells expressing the T4 (CD4) antigen, which HIV uses to attach to the cell. Chemokine co-receptors (CCR5 or CXCR4, or both) are required forvirus entry, and individuals with CCR5 deletions (i.e., “delta 32”) are less likely to become infected and, once infected, the disease is more likely to progress slowly.

Once it enters a cell, HIV can replicate and cause cell fusion or death. A latent state is also established, with integration of the HIV genome into the cell’s genome. The cell principally infected is the CD4 (helper-inducer) lymphocyte, which directs many other cells in the immune network. With increasing duration of infection, the number of CD4 lymphocytes falls. Some of the immunologic defects, however, are explained not by *quantitative* abnormalities of lymphocyte subsets but by *qualitative* defectsin CD4 responsiveness induced by HIV. [7]

CD4 + cells

The primary immunopathogenic lesion in HIV infection involves CD4+ T cells, and the range of CD4+ T cell abnormalities in advanced HIV infection is broad. The defects are both quantitative and qualitative and ultimately impact virtually every limb of the immune system, indicating the critical dependence of the integrity of the immune system on the inducer/helper function of CD4+ T cells. In advanced HIV disease, most of the observed immune defects can ultimately be explained by the quantitative depletion of CD4+ T cells. However, T cell dysfunction can be demonstrated in patients early in the course of infection, even when the CD4+ T cell count is in the low-normal range. The degree and spectrum of dysfunctions increase as the disease progresses.[8]

Albumin level and Immuno suppression

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 constraints.

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While they remain as main clinical markers, they do not fully explain anindividual's prognosis. There is a need to identify and establish efficacy of alternate prognostic markers of immunosuppression. [9]

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.

Low levels of serum albumin have been associated with higher rates of mortality in different acute and chronic conditions. 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, independant of CD4 cell counts and HIV RNA titre.[10,11]

Serum Albumin Level could prove to be a very useful, cheap and easilyavailable supportive 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.[12]

This study was planned to evaluate Serum albumin level in patients suffering from HIV/AIDS and to evaluate other markers of immunosuppressionin HIV/AIDS patients like Albumin/Globulin ratio, Hematocrit and Platelet count and to correlate between serum albumin levels, CD4+ cell count and other markers of immunosuppression.

Aims & Objective

1. To evaluate Serum albumin level in patients suffering from HIV/AIDS.
2. To evaluate other markers of immunosuppression in HIV/AIDS patients like Albumin/Globulin ratio, Hematocrit, and Platelet count.
3. To correlate between serum albumin levels, CD4+ cell count and other markers of immunosuppression.

Material & Methods

This study was conducted at JLN Medical College and Hospital, Ajmer (Raj.) on 200 HIV/AIDSpatientspresentingtoand registered at ART Centre JLN Hospital, AjmerduringtheperiodofOct, 2014 to Jan, 2016.

Adetailedhistory,clinicalexaminationandlaboratoryinvestigationsincludingHaemoglobin,TotalandDifferentialWBCCounts,Hematocrit,LiverFunctionTestswithSerumAlbuminLevel,RenalFunctionTests,CD4+CellCounts,UrinaryAlbumin& HIVTridot testwasdone.

StudyDesign:Cross sectional study.

Inclusion criteria

HIVinfected/AIDSpatients>18yearsofage.

Exclusion criteria

- Anypre-existinghepatobiliarydiseasecausingdecreaseinalbuminlevel.
- Anypre-existingrenaldisease/chronickidneydiseasecausingdecreaseinalbuminlevel.
- Anypre-existinggastrointestinaldiseasecausingdecreaseinalbumin level.
- Anyclinicalevidenceofcongestivecardiac failure
- Anyclinicalevidenceof shock
- Anyh/oburnsinlast21days

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Result

Table 1. Age wise distribution of cases

Age in years	No of cases	% of cases
<20	2	1.0
21-30	45	22.5
31-40	59	29.5
41-50	78	39.0
51-60	13	6.5
61-70	3	1.5
Total	200	100.0

Table 2. Sex wise distribution of cases

Sex	No of patients	%
Male	147	73.5
Female	53	26.5
Total	200	100

Table 3:

Markers	Mean value	± SD
CD4count	378.4	23.7
Albumin level	3.21	0.68
Platelet Count [Lacs]	1.28	0.02
Albumin/Globulin Ratio	1.77	0.13
Hematocrit [%]	44.57	5.12

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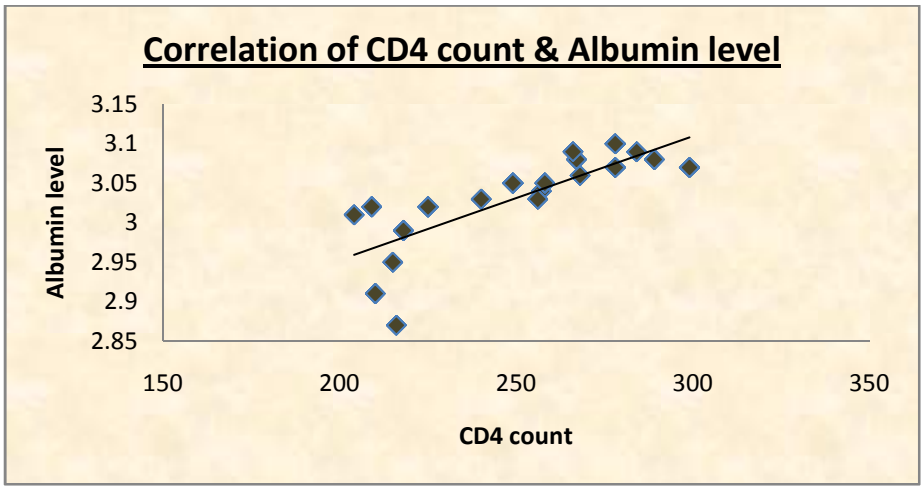
Figure 1



Pearson correlation coefficient [r]=0.784, P<0.001, Significant positive correlation.

Discussion

With the aim and objective to evaluate Serum albumin level in patients suffering from HIV/AIDS, to evaluate other markers of immunosuppression in HIV/AIDS patients like, Albumin/Globulin ratio, Hematocritand Platelet count. And to correlate between serum albumin levels, CD4+ cell count and other markers of immunosuppression.

Cases studied

This study was conducted on 200HIV/AIDSpatients.

While Lang et al[14] conducted a large study on a total of 25 522 who were HIV positive. In the study of Tabarsiet al[15] 111 HIV positives were included. Olawumiet al[13] studied on one hundred and eighty-five patients and Koethe et al[16] enrolled 142 HIV positive participants

Age

In this study out of total 200 participants most were 20-50 years 182 [91%] of age, and only 16 [8%]were above 50 years if age and 2 [1%] cases were less than 20 years. Majority was in the age of 41-50 years 78 [39%].

The mean age was 42.67 ± 5.8 years.

In the study of Lang et al themean age was 47.5 ± 3.4 years, whilein Tabarsi et al[15] study the mean age for all 111 HIV patients was 38 ± 9 years (range 22–70) Olawumi et al[13] One hundred and eighty-five patients aged 37 ± 10 years were recruited to this study and in the study of Koethe et al[16]the mean age was 41.6 ± 2.2 years

Sex

In our study of the total cases predominantly were males 147 [73.5%] and females were only 53 [26.5%]. Male : female ratio was 2.77 : 1.

Similarly in the study of Tabarsiet al[15] majority 107 (96.3%) were men but in the study of Olawumi et al[13] the ratio was pretty close (91 male and 94 female) and in the study of Lang et al the males were in majority 67%.

Clinical features

The most common presenting complaint was fever seen in 115 [57.5%] cases followed by cough and weight loss in 87 [43.5%] and 77 [38.5%] respectively. Breathlessness was seen in 63 [31.5%]

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cases and diarrhea in 41 [20.5%]. 11 [5.5%] cases were having seizures.

Similar in the study of Lang et al fever was the commonest feature [68%] followed by weight loss [53%].

In the study of Olawumiet al[13] fever was seen in 75% cases and weight loss was in 42% cases but diarrhea was in 47% cases.

But Koetheet al[16] found in their study that fever was seen in only 24% cases while weight loss was the predominant symptom seen in 57% cases.

Opportunistic infections

Opportunistic infections were seen in large no of cases. The most common was oral candidiasis seen in 81 [40.5%] cases followed by PulmonaryTB in 75[37.5%] and esophageal candidiasis in 32 [16%] cases. Toxoplasmosis was seen in 11 [5.5%] cases. Lang et al[14] found opportunistic infection in 67% of cases, oral candidiasis seen in [38%] cases and Pulmonary TB in [17%], Similarly In the study of Tabarsi et al[15]oral candidiasis seen in [59%] cases and Pulmonary TB in [12%], but Koethe et al[16] observed low opportunistic infection, oral candidiasis seen in only 13% cases.

High risk behavior

High risk behavior was enquired in the cases. The most common was unprotected heterosexual behavior seen in 108 [54%] of the cases. 79 [39.5%] had history of unsafe transfusion. IDU users were 19[9.5%] and two cases had MSM. Lang et al found unprotected heterosexual behavior in majority of the cases [68%] and MSM in 3%.But in the study of Tabarsi et al[15]unprotected heterosexual behavior was seen in only 32% cases and 54% were IDU.

Olawumiet al[13] found unprotected heterosexual behavior in 57 % cases and unsafe transfusion in 18%.

Albumin

In our study the mean albumin level was 3.21 ± 0.68 , There was Significant positive correlation between CD4 count and albumin level.[r]=0.784, P<0.001.

In the study of Lang et al[14] it was observe that those with lower levels of albumin also had lower CD4 cell counts, higher viral load. The overall median number of albumin measures was 8 (IQR 3–18), including 10 (4–22) measures among survivors, and six (3–14) among those who died during follow-up.

Tabarsi et al[15] found that albumin levels were significantly lower in patients with a poor outcome 5.2 ± 1.2 versus 26.7± 4.5 g/L).

Olawumiet al[13] observed that mean pretreatment and post-treatment serum albumin levels were 32 ±5.4 and 37.7 ± 3.7 mg/L, respectively. There were significant positive correlations between pretreatment albumin and both pretreatment CD4 cell count.

Koetheet al[16] found that the associations of baseline albumin, ferritin and hs CRP with mortality were statistically significant.

CD4+

In our study CD4 count was tested in all the cases. In majority cases it was between 200-500 [96, 48%] and in 63 [31.5%] it was less than 200, however it was above 500 in 41 [20.5%] cases. The mean CD4 count was 378.4 ± 23.7.

In the study of Tabarsiet al[15] the mean CD4 counts were 176 and 140 in patients with good outcomes and poor outcomes, respectively.

A correlation was not found between CD4 count and outcome (P > 0.05). Furthermore, a CD4 count above 100 and below 100 did not affecttreatment outcome.

Olawumiet al[13] observed that the mean CD4 cell count was 215 ±120 cells/mL pretreatment and 372 ±180 cells/mL post-treatment. The post-

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treatment CD4 cell count was significantly higher than the pretreatmentcount. There were also significant positive correlations betweenpost-treatment albumin and posttreatment CD4 count up to a count of 700 cells/mL but the positive correlation between increase in serum albumin and increase in CD4 count was just below statistical significance. The sensitivity of serum albumin against CD4 count was 91.5%, the specificity was 40%, and the positive predictive value was 96.15%

Koethe et al[16] observed that the CD4+ lymphocyte counts below 50 cells/mm3 An interval increase in albumin remained a significant predictor of mortality and the composite endpoint while interval changes in phosphate, ferritin and hsCRP remained non-significant.

Conclusion & Summary

1. Males were more common in the study [73.5%] indicates more sexual promiscuity in males.
2. More people presented with a late onset of illness(> 6 months)
3. Most Common opportunistic infection was oral candidiasis.
4. Heterosexual behavior most common risk factor of our study patients.
5. There was a strong and significant direct correlation between CD4 count and Albumin level in cases indicating that albumin could be used as a supplementary marker for immunosuppression in HIV/AIDS patients.
6. Platelet count is not significantly correlated with CD4 count thus it cannot be used as marker of immunosuppression in HIV patients.
7. There was a strong and significant direct correlation between CD4 count and Albumin/ Globulin ratio.
8. Hematocrit % is not significantly correlated with CD4 count thus it cannot be used as marker of immunosuppression in HIV patients.

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