ISSN- O: 2458 - 868X, ISSN–P: 2458 – 8687
Index Copernicus Value: 49. 23
PubMed - National Library of Medicine - ID: 101731606

International Journal of Medical Science and Innovative Research (IJMSIR)
IJMSIR : A Medical Publication Hub
Available Online at: www.ijmsir.com
Volume – 4, Issue – 2, March - 2019, Page No. : 272 - 276

Serum Albumin Level as a Surrogate Marker of Immune Suppression in Patients with HIV/AIDS: An Observational Study at A Tertiary Care Centre.

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Type of Publication: Original Research Paper
Conflicts of Interest: Nil

Abstract

There is progressive failure of the immune system in patient with HIV/AIDS, which allows life threatening opportunistic infections and cancers. CD4 cell count and HIV RNA viral load are most widely used markers to indicate disease progression. These methods are costly so there is need for a cheap but useful marker. Therefore in this study we want to predict Serum albumin level as a effective and easily available surrogate marker of disease in HIV/AIDS patients.

Method: It was an observational study conducted in the Department of Medicine and ART clinic, S.M.S. Medical College and Hospital, Jaipur, from June 2017 to December 2018. 200 HIV/AIDS patients taking Anti Retroviral therapy were included in the study after obtaining written informed consent. Along with other investigations CD 4 count and S.Albuin was measured at the time of admission and at 6 month follow up. Data were analyzed statistically.

Results: CD4 count below 200 was seen in 22% at baseline and in 17.5% at 6 month follow up. The difference in baseline S.Albumin and at 6 months follow up was statistically significant (X^2 =12.586, p-0.01). S. Albumin was found to be significantly correlated with CD4 count at baseline (r = 0.76, p<0.001) and at 6 month (r = 0.71, p<0.001) respectively.

Conclusion: Serum albumin can serve as a low cost, effective and easily available surrogate marker in lieu of CD4 count in settings where frequent assessment of CD4 cell count and HIV viral load is not possible.

Keywords: HIV, AIDS, CD4 cell count, S. Albumin, Disease progression

Introduction

Human immunodeficiency virus is a lentivirus, a member of the retrovirus family that causes acquired

immunodeficiency syndrome. There is progressive failure of the immune system in the patient which allows life threatening opportunistic infections and cancers to thrive[1]. HIV infection/AIDS is a global pandemic, with cases reported from virtually every country. More than 95% of people living with HIV/AIDS reside in low- and middle-income countries; 50% are female, and 2.1 million are children <15 years[2].

CD4+cell counts and HIV RNA levels have been widely accepted as the most powerful indicators of HIV disease progression.[3] 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.[4] As an alternative to these two tests, many other biological and biochemical markers can be used, like lymphocyte count, serum albumin level, serum albumin: globulin ratio, C-Reactive protein, serum CD8 cell, p24 antigen etc.[5]

Albumin is the most abundant protein in human body. It is produced in liver and has a half-life of approximately 21 days. It is a monomeric soluble protein of 584 amino acids. Reference serum value range is 3.5–5.5 gm/dl[6]. It functions to maintain oncotic pressure and helps in transport of hormones, free fatty acids, unconjugated bilirubin, drugs and is also a negative acute phase protein being downregulated in inflammatory states. Some recent studies suggested that low level of serum albumin is associated with HIV/AIDS disease progression. Other studies have suggested that albumin could serve as a surrogate marker of HIV disease progression in resource limiting settings. It can be useful, cheap, and easily available test for predicting severity of HIV infection, pre treatment assessment and clinical monitoring of response to Anti Retroviral Therapy. However there is still dearth of evidence correlating CD4 cell count & serum albumin level in Indian population. Therefore in this study we want to predict Serum albumin level as a effective and easily available surrogate marker of disease in HIV/AIDS patients.

Material and methods

It was a hospital based prospective observational study conducted in the Department of Medicine and ART clinic, S.M.S. Medical College and Hospital, Jaipur, from June 2017 to December 2018.

Sample size: Minimal sample size required was 200 at 95% Confidence Interval and 80% power to detect the correlation (r=0.208) between serum albumin level and CD4 cell count.

200 HIV/AIDS patients taking Anti Retroviral therapy were included in the study

after obtaining written informed consent. Patients with liver disease, renal disease, congestive heart failure, pregnancy, history of burn in last 21 days and having history of blood products/albumin transfusion in last 20 days were excluded from the study. A detailed history, clinical examination and laboratory investigations including haemoglobin, total and differential WBC Counts, platelet count, liver function tests with serum albumin level, renal function tests, CD4+ cell counts, & HIV Elisa & western blot, HIV RNA estimation were done.

Repeat measurements of serum albumin and CD4+ cell count was done at 6th month follow up. Data were entered in MS Excel sheet and statistically analyzed. A p value less than 0.05 was considered as significant.

Results

Most of the study subjects were between the age group of 26-45 years. Age distribution was almost equal in male and female. Mean age in study population was 35.79±7.32 years. Mean age in female group was 35.90±7.13 years

while in males it was 35.70±7.48 years. 29.3% males and 41.4% females had BMI <18.5 Kg/m^2 while 70.7% males and 58.6% females had normal BMI (18.5-24.9 Kg/m^2). Overall one-third (34.5%) of study subjects were underweight (BMI< 18.5 kg/m^2) while rest 65.5% were with normal BMI (18.5-24.9 kg/m^2). Mean BMI for male was 19.84±1.94 kg/$m^2$and for female it was 19.23±1.82 kg/m^2. Mean BMI of study subjects was 19.67±1.96 kg/m^2.(Table 1)

Table 2 shows opportunistic infections in study subjects. Opportunistic infections were observed in 60 (30.0%) cases. Out of these pulmonary TB (33.3%) was the most common opportunistic infection followed by oral candidiasis (28.3%), Herpes Zoster (10.0%), extrapulmonary TB (10.0%) and esophageal candidiasis (8.3%).

CD4 count below 200 was seen in 22% at baseline and in 17.5% at 6 month follow up. CD4 count was between 200-500 in 65% cases at baseline and in 71.5% cases at 6 months follow up. Though the difference in baseline CD4 count and at 6 month follow up was statistically not significant in our study (X^2 =4.622, p-0.2). (Table 3)

Mean S. Albumin as baseline was 2.97±0.60 g/dl while at 6 months follow up it was 2.99±0.52 g/dl. The difference in baseline S.Albumin and at 6 months follow up was statistically significant (X^2 =12.586, p-0.01). (Table 4)

Baseline S. Albumin was found to be significantly correlated with baseline CD4 count (r = 0.76, p<0.001). (Fig 1) S. Albumin at 6 months was also found to be significantly correlated with CD4 count at 6 months (r = 0.71, p<0.001). (Fig 2)

Discussion

HIV/AIDS is a disease that is a source of concern in our state of Rajasthan. The tests used for assessing AIDS stage and monitoring response to therapy are CD 4 cell count and viral load analysis. Majority of the patients in our state cannot afford to pay for these investigations. There is therefore a need to look for other, cheaper tests that can be used to monitor response to treatment. We have tried to find use of S. Albumin as an alternate marker for HIV/AIDS.

This study was conducted on 200 HIV/AIDS patients while shah et al.[4] conducted a study on 291 who were HIV positive. In the study done by S S Sharma et al[7] 100 cases were included. Olawumi et al[6] studied on 185 HIV positive cases.

In our study out of total 200 participants 185 [92.5%] subjects were in the age group between 25 to 55 years, while only 1 [0.5%]was above 55 years of age and 14 [7%] cases were less than 25 years of age. Majority 39 % were in the age of 26-35 years.

Mean age in female group was 35.90±7.13 years while in males it was 35.70±7.48 years.

Overall mean age was 35.79±7.32 years. Main reasons behind this age group are high risk sexual behaviour, social stigma & lack of awareness about the disease. Our results were comparable to studies done by Oluwami et al[6] (mean age was 37 ± 10 years), Shah et al[4] (mean age was 38.3 ± 7.9 years) and that done by S S Sharma et al[7] (mean age was 36.9 ± 10.7 years). Mean age in our study was lower than that observed by Mehta et. al[8] (mean age was 47.5 ± 3.4 years).

In our study out of the total 200 cases, males were 116 [58%] and females were 84[42%]. Male:female ratio was 1.38:1. Similarly in the study of Mehta et al[8] majority of patients (75.7%) were male and 24.3% were female. In the study done by Oluwami et al[6] male patients were 49.1% while female patients were 50.9%. In study done by Shah et al[4] 75% were male and 25% were female and in a study done by S.S. Sharma et al[7] male and female patients were

72 % and 28% respectively. The gross difference in presentation of male and female is due to multiple risk factors like males are migrators and primary disease spreaders. It can also be due to poor health seeking behaviour of females.

Opportunistic infections were seen in 60 (30%) cases. The most common was pulmonary TB seen in 20 [33%] cases followed by oral candidiasis 17[28.3%] and extrapulmonary TB in 6[10%] cases. Esophageal candidiasis was seen in 5(8.3%) and herpes zoster was seen in 6 [10%] cases. Similar results were seen by Prahladrao SH et al[9] they found opportunistic infections in 57.5% of cases. Oral candidiasis was seen in 81 [40.5%] cases and Pulmonary TB in 75[37.5%]. In the study done by SS Sharma et al[7] most common opportunistic infection was oral candidiasis in 24% cases. Pulmonary TB was seen in 6% and extrapulmonary TB in 12 % cases. Manish Ghete et al[10] reported incidence of opportunistic infection to be 35.7 per person years and the most common infection in his study was Tuberculosis.

Tuberculosis and oral candidiasis are the most commonly reported HIV-related opportunistic infection in India.[11]This high incidence of opportunistic infection may be due to social stigma and lack of awareness of disease that's why much work is required in public health programs to improve patient awareness so that more people can be detected in asymptomatic stages. Delayed diagnosis of illness increases chances of poor response to therapy as well[8.]

In our study 22 % cases had CD4 count below 200/µl, 43% cases it was below 350/µl and in 13% cases CD4 count was above 500/µl. On follow up in 17% cases CD4 was below 200/µl, in 41% was below 350/µl, and in 11% cases CD4 count was above 500/µl. In the study of K. Suresh Babu,[12] the baseline CD_4 count of both the genders was less than 250/µl. In poor communities, the patients accept a HIV test after suffering for a long time and tried on all kinds of home remedies without success. During this time their CD_4 cell counts progressively declined. 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 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 among them, with correlation coefficient of 0.76 (baseline) and 0.71 (follow up) .Both the results were statistically significant (p values <0.001). Mean albumin level at baseline was 2.97±0.6 and at 6 months follow up it was 2.99 ±0.52. Olawumi et al[6] observed that mean pre-treatment and post-treatment serum albumin levels were 3.20±0.54 and 3.70±0.37 gm/dl respectively which was higher than that observed in our study.

There were significant positive correlations between pre-treatment albumin and pre-treatment CD4 cell count and between post-treatment albumin and post-treatment CD4 cell count.

This study has shown that serum albumin could be a good index of severity of disease, because pre treatment albumin level correlates well with pre-treatment CD4 cell count, which is the traditional marker of severity. Furthermore, the mean level of pre-treatment albumin decreased with decreasing CD4 cell count and later stages of HIV/AIDS.

Conclusion

In conclusion, we can say that serum albumin can serve as a low cost, effective and easily available surrogate marker in lieu of CD4 count in settings where frequent assessment of CD4 cell count and HIV viral load is not possible.

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Legends Tables and Figure

Table 1: Demographic characteristics of the patients

Demographic characteristics	Female (n=84)		Male (n=116)		Total (n=200)	
	Number	Percentage	Number	Percentage	Number	Percentage
Age (years)						
<25	5	5.9	9	7.8	14	7
25-45	72	85.8	97	83.6	169	84.5
45-65	7	8.3	10	8.6	17	8.5
BMI (Kg/m^2)						
<18.5	35	41.4	34	29.3	69	34.5
18.5-24.9	49	58.6	82	70.7	131	65.5

Table 2: Opportunistic infections in study subjects

Opportunistic infections	No.	%
Cryptococcal meningitis	1	1.7
Esophageal candidiasis	5	8.3
extrapulmonary TB	6	10.0
Herpes zoster	6	10.0
Oral candidiasis	17	28.3
Pneumocystis	1	1.7
Pulmonary TB + Oral candidiasis	4	6.7
Pulmonary TB	20	33.3
Total	**60**	**100.0**

Table 3: CD4 Counts in patients of HIV/AIDS

CD4 count	CD4 count level				Chi-square P value
	At baseline		At 6 months		
	No.	%	No.	%	
< 200	44	22.0	35	17.5	4.622
200-350	87	43.5	82	41.0	
351-500	43	21.5	61	30.5	P =0.2
>500	26	13.0	22	11.0	Not sig
Total	**200**	**100.0**	**200**	**100.0**	

Table 4: S. Albumin levels at baseline and 6 months follow up in patients of HIV/AIDS

S. Albumin (gm/dl)	Baseline		At 6 months		Chi-Sq P value
	No.	%	No.	%	
1.5-2.0	23	11.5	12	6.0	12.586
2.1-2.5	22	11.0	27	13.5	
2.6-3.0	59	29.5	49	24.5	P 0.01
3.1-3.5	59	29.5	87	43.5	significant
3.6-4.0	37	18.5	25	12.5	
Total	**200**	**100.0**	**200**	**1000**	

Figure 1: Scatter plot showing correlation between CD4 count and S. Albumin at Baseline

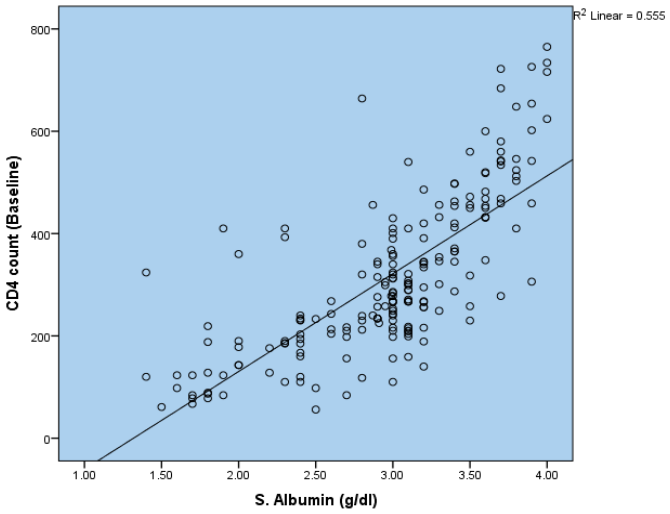

Figure 2: Scatter plot showing correlation between CD4 count and S. Albumin at 6 months