

Serum protein, albumin, globulin levels, and A/G ratio in HIV positive patients

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ABSTRACT

Estimating serum total protein & serum albumin level assesses the nutritional status of the patient. Malnutrition is an important complication of HIV infection. Opportunistic infections not only cause altered body metabolism but are also associated with reduced oral intake, which seems to be the most important determinant of weight loss. The present study attempts to assess the following:-

1. The protein status in HIV positive patients.

2. If it is useful as a prognostic tool.

The study demonstrates a significant increase ($p < 0.01$) in serum total protein in morbid group as compared to controls. The mean serum total protein level in HIV positive patients was 7.43 ± 0.43 gm% (control group = 7.07 ± 0.22 gm%). The serum albumin levels (mean = 2.67 ± 0.34 gm%) were decreased in morbid group as compared to control (4.45 ± 0.26 gm %), which was found to be statistically highly significant ($p < 0.001$). The serum globulin levels (mean = 4.76 ± 0.41 gm %) were increased in HIV positive patients as compared to controls (2.6 ± 0.29 gm %). This increase was statistically highly significant ($p < 0.001$). The mean serum A: G ratio in the control group was found to be 1.7 ± 0.26 whereas in HIV positive patients it was reversed (0.56 ± 0.1), which was statistically highly significant ($p < 0.001$), according to the present study. The serum albumin level (< 3 gm%) can be used as a prognostic indicator.

Key words: Total protein; albumin; globulin; A: G ratio; and HIV/AIDS.

INTRODUCTION

Diarrhoea is a common presenting feature of AIDS. Many patients with AIDS who develop diarrhea have some degree of jejunal villous atrophy and over 70% have some evidence of malabsorption. In AIDS diarrhea is often associated with reduced serum albumin (< 10 gm/lit), probably due to hypercatabolism, though other factors may contribute, including malabsorption and a protein losing enteropathy as indicated by an increase in faecal alpha-1-antitrypsin. Severe weight loss is common among AIDS patients. HIV wasting syndrome is defined as weight loss of over 10 % of baseline with no other cause over 30 days or more

either diarrhea or weakness with fever. In weight loss of malnutrition the fat tissue is preferentially depleted and muscle protein is preserved. In contrast acute infection, trauma, burns tend to be accompanied by protein catabolism and a negative nitrogen balance. Although serum total protein estimation has limited diagnostic importance when compared to albumin because of the compensatory increases in other serum proteins (the globulins) during infections, its relevance in the evaluation of patients with some clinical conditions such as malnutrition, malignancy, renal and liver diseases & immune disorders cannot be ignored [Gray CH, *et al.*, (1985)].

MATERIAL AND METHODS

Clinical Material

The present work, on "Serum protein, albumin, globulin levels and A:G ratio in HIV positive patients", was carried out on 40 HIV positive patients admitted in Medicine wards in Government Medical College, Aurangabad, Maharashtra. Forty healthy & HIV negative control cases were included in the study. Mean age of morbid (27 males & 13 females) & control cases (28 males and 12 females) was approximately 35 years.

Inclusion criteria

HIV positive patients were included.

Exclusion criteria

Patients suffering from diabetes, renal disorders, and cases with fever & vomiting were excluded.

Methods

The serum samples were collected from the Department of Microbiology after they were confirmed to be HIV positive by the ELISA Recombigen Test and Rapid Capillus Latex Agglutination Test. Blood samples from healthy individuals were collected in the OPD, processed for HIV testing in the Department of Microbiology and after confirming HIV negativity the samples were analyzed biochemically. All blood samples were collected in plain bulbs. The biochemical investigations were performed on the fully automated analyzer – Erba Superstat 919, except serum globulin and A: G ratio, which was calculated mathematically. All the values were calculated in gram%. The data were statistically analyzed using 't-test'. Following table shows the method employed with normal values of all biochemical parameters tested.

Biochemical Parameter	Method	Wavelength (nms)	Formula	Normal Value (gm%)
Total Protein	Biuret	546	A (T) * Conc of S (6 gm%)	6 – 8.3
Serum Albumin	BCG (Bromo Cresol Green)	659	A (T) * Conc of S (6 gm%) A (S)	3.2 – 5.3
Serum Globulin	Enzymatic method (Doumas et al)		(serum total protein) – (serum albumin)	1.8 – 3.6
A: G			serum albumin/serum globulin	1.5:1 – 2:1

RESULTS

The mean serum total protein level in control group was 7.07 ± 0.22 gm% which was increased to 7.43 ± 0.43 gm % in HIV positive patients; statistical analysis showed significant ($p < 0.01$) relationship between control & morbid groups. The mean serum albumin level in the control group was 4.45 ± 0.26 gm % which was found to be decreased upto 2.67 ± 0.34 gm % in HIV positive

Table 1: Mean Age & Sex Differentiation in Control and Morbid Group

S. No	Group	No of males	No of Females
	Control	35.17	28
	HIV Positive Cases	34.65	27

Table 2: Mean \pm SD in control & morbid groups

S. No	Biochemical Parameter	Max-Min Range [Control]	Max-Min Range [Morbid]	Mean \pm SD (gram %)	
				Control Group	Morbid Group
1.	Total Protein	7.5-6.7	8.3-6.9	7.07 \pm 0.22	7.43 \pm 0.43
2.	Albumin	5.0-4.0	3.2-2.4	4.45 \pm 0.26	2.67 \pm 0.34
3.	Globulin	3.3-2.1	5.6-3.9	2.6 \pm 0.29	4.76 \pm 0.41
4.	A:G Ratio	2.3-1.2	0.7-0.3	1.7 \pm 0.26	0.56 \pm 0.1

Thus following is evident from the above table –

The mean serum total protein level in control group was 7.07 \pm 0.22 gm% which was increased to 7.43 \pm 0.43 gm % in HIV positive patients; statistical analysis showed significant ($p < 0.01$) relationship between control & morbid groups.

patients and the decrease was statistically highly significant ($p < 0.001$). The mean serum globulin level in the control group was 2.6 \pm 0.29 gm % which was increased to 4.76 \pm 0.42 in HIV positive patients. It was found to be statistically highly significant ($p < 0.001$).

The mean serum A: G ratio in the control group was 1.7 \pm 0.26 whereas in HIV positive patients it was found to be reversed; values being 0.56 \pm 0.1 ($p < 0.001$).

DISCUSSION

According to the present study mean serum total protein level in control group was 7.07 \pm 0.22 gm% which was increased to 7.43 \pm 0.43 gm % in HIV positive patients ($p < 0.01$). Ulrich R. et al (1989) demonstrated the average value of total serum protein for HIV positive patients was 73 gm/lit whereas for serum albumin it was 38 gm/lit.¹⁴

The mean serum albumin level in the control group in the present study was 4.45 \pm 0.26 gm % which was found to be decreased upto 2.67 \pm 0.34 gm % in HIV positive patients ($p < 0.001$). Hypoalbuminemia and was reported by Schnieder mann D et al (1987) (3.2 gm %), Dworkin B., et al., (1987) (3.0 gm%), Dworkin B., et al., (1985) (mean = 3.3 gm/dl)^{13, 5, 4}. Guenter P. et al., (1993) observed that the serum albumin levels and weight loss were related to CD 4 counts. They stated that the relative risk for subjects with low serum albumin levels (< 3.5 gm/dl) was 3.6 times greater ($p < 0.021$) than that for subjects with normal serum albumin

levels (> 3.5 gm/dl) and CD 4 counts.⁹ Fernandez p et al (1995) evaluated the serum albumin levels < 30 gm/lit were related with a poor prognosis.⁷ Wilcox C. M. et al (1996) stated, that in a study of 71 HIV positive patients, death was strongly associated with reduced serum albumin concentration.¹⁵ Colin J. F. et al (1999) stated that HIV positive patients had lower serum albumin levels ($p = 0.0009$).³ Joel E. Gallant (2004) explained that a low albumin typically occurs at advanced stages of HIV disease and reflects poor nutritional status. However, the elevated total protein and globulin fraction can occur in otherwise healthy HIV-positive individuals. It probably reflects a generalized, polyclonal gammopathy, with increased antibody production, which is an attempt on the part of the immune system to compensate for cellular immunodeficiency.

The mean serum globulin level in the control group was 2.6 \pm 0.29 gm % which was increased to 4.76 \pm 0.42 in HIV positive patients ($p < 0.001$). The increase in the anion gap may be associated with increased level of IgG (hyperglobulinemia).

Hyperglobulinemia in HIV patients was demonstrated by studies by Quensel A et al., (1994) & Miguez – Burban M.J. et al (1995) ($p = 0.003$).^{12, 11} Hyperglobulinemia seen in HIV positive patients may be due to increased levels of IgA and IgG in this disease. Ball S.G. (1994) stated that AIDS diarrhea is often associated with reduced serum albumin, as low as 10 gm/lit in severe cases, probably due to hypercatabolism, though other

factors may contribute including malabsorption and protein losing enteropathy. He also states that polyclonal hyperglobulinemia may be sufficient to raise the total protein typically by some 10 to 15 gm/lt.¹

Khot V.V. (1999) concluded that the total serum protein levels and serum globulin levels in HIV positive alcoholics and HIV positive non alcoholics were increased; serum albumin levels & A: G ratio were reduced in the above groups, but the differences were not statistically significant ($p < 0.05$). She stated that the total serum proteins levels ($p < 0.001$) & serum globulin levels ($p < 0.001$) in HIV positive non alcoholics were higher than HIV negative non alcoholics. Serum albumin levels were significantly decreased in HIV positive non alcoholics compared to HIV negative non alcoholics ($p < 0.001$). When HIV positive alcoholics were compared with HIV negative non alcoholics the total protein levels in HIV positive alcoholics was increased ($p < 0.001$) whereas serum albumin levels were decreased in HIV positive alcoholics ($p < 0.05$). Serum globulin levels were increased in HIV positive alcoholics ($p < 0.001$).¹⁰ The present study demonstrates mean serum A:G ratio to be 1.7 ± 0.26 (controls) whereas in morbid group it was found to be reversed; values being 0.56 ± 0.1 ($p < 0.001$). Although serum total protein estimation has limited diagnostic importance when compared to albumin because of the compensatory increases in other serum proteins (the globulins) during infections, its relevance in the evaluation of patients with some clinical conditions such as malnutrition, malignancy, renal and liver diseases and immune disorders cannot be ignored [Gray CH, *et al.*, (1985)]. Decrease in serum total protein in HIV infection has

been associated with either increased losses &/or catabolism or as a result of reduction in intake &/or absorption due to sores in the mouth, pharynx &/or oesophagus, fatigue, depression and side effects of medications (Macallan DC) (1999).

Guardia J. A. *et al.*, (1997) concluded that in HIV positive patients the serum albumin level was on an average 2.3 gm %. The mean value of serum globulin in HIV positive patients was 3.1 gm %. They concluded that globulins play an important role in maintaining oncotic pressure in low albumin states.⁸ Cirasino L. *et al.* (1996) demonstrated in patients wherein the survival was significantly reduced for those groups which at the beginning of the followup showed CD 4 lymphocyte count < 240 /cubic mm, serum albumin < 4.13 gm/dl ($p = 0.04$) and serum IgA > 2.5 gm/dl ($p = 0.043$).²

CONCLUSIONS

Though the serum albumin levels were decreased in HIV positive patients, the serum globulin levels were increased, which resulted in the total serum protein levels remaining apparently in normal range. The serum globulin was increased above the upper limit of normal in all HIV positive patients. The A: G ratio was found to be reversed in HIV positive patients. Globulins play an important role in maintaining the oncotic pressure in low albumin states in these patients. HIV positive patients with serum albumin lower than 3 gm % generally have a poor prognosis; hence the serum albumin level can be used as a prognostic indicator. These depressed albumin levels could reflect the poor nutritional status, catabolic state of chronic disease evidenced by significant weight loss.

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