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# SERUM PROTEIN ALTERATIONS IN MALIGNANT NEOPLASIA

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## ABSTRACT

Malignant neoplasia is thought to develop through multifactorial gene stimulations which leads to marked variations in plasma proteins. The study aims at the quantification of serum albumin and different globulin fractions in 28 multiple myeloma and 25 other hematological cancer and compare the alterations with that of 40 age and sex matched normal subjects. Serum albumin and total proteins were estimated by spectrophotometric methods. Quantitation of globulin fractions were done by scanning the electrophoretogram by densitometry. Hypoalbuminemia and hypergammaglobulinemia were evident both in multiple myeloma and leukemia compared to normal from the results of the present study. Further, decrease in albumin was statistically significant in leukemia compared to multiple myeloma. While $\alpha_1$globulins increased in leukemia, β globulins increased significantly in multiple myeloma compared to normal .The results provide evidence to support the idea that different type of globulins increase in varied types of hematological cancers. Further work needs to be carried out to allow us to understand the underlying mechanisms that has led to the increase of $\alpha_1$ or β globulins in hematological cancers and explore new tumor markers.

**KEY WORDS:** **Multiple myeloma, leukemia, α globulins, β globulins**

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## INTRODUCTION

Serum contains hundreds of proteins each with a specific set of functions which are subject to variations in concentration under different pathological conditions. One of the profound effects of malignant neoplasia is the changes in protein components, but the significance of which is still poorly understood. A number of adverse prognostic factors in hematological malignancies like Hodgkins disease include hypoalbuminemia[1], elevated $\beta_2$microglobulin, interleukins[2]. Patients with lymphoid malignancies including multiple myeloma , lymphocytic leukemia also showed elevated $\beta_2$ microglobulin[3]. Although the definite cause for the increase in globulins is not understood, it is suggestive that these proteins are derived from the neoplasm as such or from autoantibodies. The present study fits into the emerging concept of immunological responses in neoplastic diseases. The study aims at the quantification of albumin and various globulin fractions in multiple myeloma and other hematological cancers and compare the alterations with that of normal.

## METHODOLOGY

Random blood samples were obtained from 28 patients with multiple myeloma, 25 patients with other hematological tumors that include dleukemias both lymphoblastic and myeloblastic forms in red capped vacutainers. The study population was aged between 50-70 years. Serum separated was used for the estimation of total proteins by biuret method[4] and albumin by bromocresol green method[5].Serum electrophoretic analysis was performed in Helena electrophoretic apparatus, using SAS-MX serum protein kit, which separates serum proteins into 5 fractions viz., albumin, $\alpha_1$,$\alpha_2$,β,γ globulins. Quantitation of the individual fraction was done by scanning the gel at 595nm. The serum protein profile including albumin,$\alpha_1$,$\alpha_2$, β, γ globulins so obtained was compared with 40age and sex matched normal subjects. Patients with the history of hepatic and kidney dysfunctions were excluded from the study. Patients with fever in the presence of demonstrable infections were also excluded from the study. Leukemia patients who were proven to have neoplasia by bone marrow biopsy and multiple myeloma patients with M band in electrophoretogram were considered for the study. Statistical analysis was done using Welch Anova with Games Howell as a post Hoc test for intergroup comparison. For parameters with non- parametric distribution Mann Whitney test and Kruskalwallis test were done. p value less than 0.05 was considered statistically significant.

## RESULTS

Hypoalbuminemia was characteristic of both multiple myeloma patients and leukemia patients. Intergroup comparison also showed statistically significant decrease in albumin in leukemia patients compared to myeloma patients. $\alpha_1$ globulins of leukemia patients and multiple myeloma patients did not differ significantly from each other. However, it increased significantly in leukemia patients when compared to normal individuals. On comparison with normal,$\alpha_2$ globulins remained unchanged both in multiple myeloma and other hematological tumors .βglobulins were strikingly elevated in myeloma patients compared to other groups. γ globulins increased significantly in multiple myeloma and leukemia patients compared to controls, however, the increase was not significant in myeloma patients compared to leukemia patients. A:G was markedly increased in tumor patients compared to normal, further, the increase was statistically significant in multiple myeloma patients compared to other neoplastic conditions.

**Table**
***Variations of plasma proteins in multiple myeloma and leukemia patients compared to normal individuals (Mean±SD)***

| | Normal N=40 | Multiple myeloma N=28 | Leukemia N=25 |
|---|---|---|---|
| Total Protein (g/dL) | 7.01± 0.38 | 8.92 ±1.76*** | 7.16± 1a |
| Albumin (g/dL) | 3.84± 0.34 | 3.5± 0.67** | 2.44± 0.57***a |
| $\alpha_1$ Globulin (g/dL) | 0.24± 0.57 | 0.27± 0.09 | 0.34 ±0.14*** |
| $\alpha_2$ Globulin (g/dL) | 0.78± 0.11 | 0.69± 0.21 | 0.81± 0.3 |
| βGlobulin (g/dL) | 0.95± 0.13 | 1.12± 1.56*** | 0.6 ±0.27***b |
| γ Globulin (g/dL) | 1.21± 0.17 | 3.33 ±1.99*** | 2.98± 0.88***b |
| Albumin:Globulin | 3.2 ±0.54 | 2.39 ±3.73*** | 0.87± 0.29***b |

******p=0.000,*p<0.05 significantly different from normal***
***a p=0.000, b p<0.05 significantly different from multiple myeloma***

# DISCUSSION

Most tumors, including multiple myeloma, are thought to develop through multiple process, through various gene stimulations [6] .Although occurrence of marked variations in different proteins is well known in malignancies, it is not the amount of total proteins in the blood but the levels of different proteins that should be considered individually .Further, the mechanism responsible for such changes in plasma proteins have remained obscure. One of the possible mechanisms being increased catabolism of albumin,a negative acute phase protein and increased synthesis of different types of globulins in various malignancies [7]. The results of the present study clearly shows a very good correlation of hypergammaglobulinemia and hypoalbuminemia in both leukemia and multiple myeloma. While increased synthesis of a type of immunoglobulin from plasma cells results in hypergammaglobulinemia in multiple myeloma, increase in gamma globulins in luekemias may be attributed to release of antibodies against antigens released from tumor necrosis [8]. Several earlier studies have shown dyslipidemia in multiple myeloma patients[9], with increase inprebeta and betalipoproteinswhichhave beta globulins as apolipoproteins. Ig A also has the electrophoretic mobility with betaglobulinswhich explains the increase in beta globulins in multiple myeloma as observed in the present study. Serum beta 2 microglobulin, a cell membrane constituent along with HLA chains increase in conditions associated with accelerated membrane turnover or accelerated cell division[10].Several reports indicate an increase in beta 2 microglobulins in acute and chronic luekemias[11],nonHodgkins lymphoma[12] and multiple myeloma[3] which may be due to increased production or impaired excretion. Present study shows a marked increase in $\alpha_1$ globulins in leukemia and multiple myeloma patients, compared to controls. A similar observation was made in earlier studies which showed increased alpha feto proteins a type of $\alpha_1$ globulins, in malignant lymphogranulomatosis and Wilms tumor[13]. The tumor mass itself might be the source of synthesis of this protein. Increase in alpha

1,alpha2 and beta globulins in cardiac tumor patients always occurred in association with increased ESR[14].$\alpha_1$ antitrypsin a type of $\alpha_1$ globulin, gets elevated in a number of inflammatory diseases and different types of malignancies including multiple myeloma[15]. The present study highlights the role of alpha 1 and beta globulin that increase in hematological tumors which may aid the future studies aimed at exploring new tumor markers.

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