Estimation of Albumin and Globulin in Pre and Post Chemotherapy Patients

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Abstract: *Cancer is a disease caused when cells divide uncontrollably and spread into surrounding tissue. Chemotherapy is the treatment involving the use of the chemical agents to stop cancer cells from growing. Chemotherapy is the drugs treatment that uses powerful chemical to kill fast-growing cell in the body. While they are the cornerstone of cancer therapeutics, they have severe harmful side effects that sometime even prove fatal. Biochemical analysis of serum proteins are important indicators of any changes from the normal pattern and therefore can be used to study the side effects of chemotherapy. One important cost-effective biochemical assay of determining serum protein pattern is serum protein electrophoresis (SPEP), which is a simple, inexpensive technique of separating bio-molecules on the basis of their net charge, size, and shape. Serum protein electrophoresis is widely used to analyze the patients with Multiple Myeloma and other serum protein disorders. Aberration from the normal pattern of albumin and globulin is an indicator of abnormality or disease including cancer. This technique can be further utilized to study the side effects of chemotherapy by estimation of albumin and globulin in pre and post-chemotherapeutic patients. The current review explores such studies that have dealt with the biochemical estimation of albumin and globulin in cancer patients as well as the effect of chemotherapy on the level of these serum proteins. Extensive electronic search was conducted to select relevant studies and then analyzed and summarized to obtain a better understanding.*

Keywords: Albumin & globulin, pre and post, chemotherapy patients, albumin and globulin ratio

1. Introduction

Cancer is a disease caused by uncontrollable cell division and spreading into surrounding tissues. Cancer has replaced heart disease as the primary cause of death in many rich countries and comes a close second in most other countries including India (The Lancet, 2019). The top cancers that affect the Indian population are lung, breast, cervical and colorectal cancer. Treatment of cancer mainly involves three modalities, chemotherapy, radiation therapy and surgery. Though chemotherapy is an effective way to treat many types of the cancer, it also carries risk of number of side effects. Some chemotherapy side effects are mild, while other can cause serious complications including death. The side effects of the cancer chemotherapy come about because cancer cells aren't the only rapidly dividing cells; cells in the blood, mouth, intestine, trace, nose, nails, vagina, and hair are also undergoing constant division. Chemotherapy is a fundamental therapy; this means it affect the whole body by going through the blood stream. Most chemotherapeutic drugs work by impairing mitosis (cell division), effectively targeting fast-dividing cells. They prevent mitosis by various mechanisms including damaging DNA and inhibition of the cellular machinery involved in cell division (**Chemotherapy with NCI 2017**).

Normal cells that are most likely to be damaged by chemo are blood-forming cells inside the bone marrow, hair follicle, cells in the mouth, digestive tract, and reproduction system. Some chemo drugs can damage cells in the heart, kidney, lungs, bladder, and the nervous system. There are many side effects caused by chemotherapy: Fatigue, hair loss, easy bruising, bleeding, infection, anemia, low red blood cells, nausea and vomiting, constipation, diarrhea, mouth, tongue and throat problems such as sores and pain with swallowing, weight change, and fertility problems (**American Cancer Society, 2019**).

It is therefore very important to assess the damage from chemotherapy to evaluate the prognosis and overall survival of a cancer patient. One important parameter that reflects abnormalities and diseased condition is serum protein pattern. Serum proteins are proteins present in blood that serve various functions like transport of lipids, hormones, vitamins, and minerals in the circulatory system and the regulation of acellular activity and functioning of the immune system. Other blood proteins act as enzymes, complement components, protease inhibitors, or kinin precursors. The most abundant serum proteins that account for 99% of all serum proteins include serum albumin, globulins, and fibrinogen. The remainder 1% of blood proteins is composed of low abundance circulatory proteins, as well as proteins secreted by live, apoptotic, and necrotic cells. Most blood proteins are secreted by the liver and intestines except for the gamma globulins, which are synthesized by the immune system (**Hoffman et al., 2000**).

Serum proteins can be quantified by serum protein electrophoresis (SPEP), a simple inexpensive technique of separating proteins based on their net charge, size, and shape. Mainly two types of proteins are present in serum albumin and globulin protein. Globulin consists of the following five categories: alpha -1, alpha -2, beta -1, beta -2, and gamma globulin (**Gary Gilliland, et al. 2004**). Serum protein electrophoresis is an established method to diagnose Multiple Myeloma and other serum protein disorders as well as blood disorders worldwide. It's a cost effective and easy technique. Plasma/serum protein patterns are susceptible to predictable changes in response to acute inflammation, malignancy, trauma, necrosis, infarction, burns, and chemical injury (**Marshall, W.J. et al., 2004**). The total albumin/globulin is a test that compares the concentration of albumin and globulin in the blood. Albumin and globulin are proteins that are commonly found in the serum, the

liquid part of your blood that does not include blood cells or clotting component (**Zhou T, et al., 2015**).

The total albumin/globulin is a test that compares the concentration of albumin and globulin in the blood. Albumin to globulin ratio (AGR) is determined by serum protein electrophoresis and it has been used since ages to determine albumin/globulin ratio as well as total protein content, especially in the diagnosis of Multiple Myeloma or more immune-proliferative disease. Aberrant AG ratio has been correlated with a wide array of chronic diseases including cancer, rheumatoid diseases, connective tissue disorder, liver diseases, nephrotic syndrome, diabetes mellitus etc. and decreased albumin has been correlated with chronic infections, chronic liver disease, and nephrotic syndrome. Albumin is synthesized in the liver. The amount of synthesis is consistent in normal individual at 150 to 250 mg/kg/day arise in the production of 10 to 18 g of albumin daily in a 70 kg man. The liver produces albumin and the primary factors affecting albumin synthesis include protein and amino acid nutrition, colloidal osmotic pressure, the reaction of certain hormones and disease states (**Walker HK, Hall WD, et al., 1990**).

Thus, AGR test is an important indicator of physiological condition of an individual and any abnormality from the normal range indicates disease. In general, an albumin and globulin ratio between 1.1 and 2.5 is considered normal. The total volume of albumin in the blood is commonly around 3.4 to 5.4 g/dl, and the total volume of globulin will be about 2.0 g/dl to 3.9 g/dl. A number of studies have been done to evaluate the role of AGR in the diagnosis and prognosis of cancer. In one such study, the AGR was determined to evaluate the association between AGR and overall survival (OS). It was investigated by Kaplan- Meier and Cox regression methods. For validation, AGR was recycled to calculate the prognosis of small-cell lung cancer(SCLC) in another independent group. According to multi-variant analysis, AGR was an independent prognostic factor for overall survival (OS) of SCLC patients in the testing group. (HR, 1.35, 95% Cl: 1.01 -1.81, p=0.046). in the validation, AGR was also documented as predictive factor for OS (p<0.001), and the high exposer of SCLC in the low AGR group was 1.43 times higher than that in the high AGR group (HR, 1.43, 95% cl: 1.05 – 1.94, p=0.22). Thus, it was concluded by the study that AGR is an independent prognostic marker in SCLC patients (Ting Zhou et al., 2016).

Serum tumor markers were evaluated in another study to see response to chemotherapy in cancer patients. Is this study, the researcher evaluated the biochemical and tumor markers post chemotherapy among breast cancer patients. There were prominent fluctuations in serum parameters due to the side effects of chemotherapy highlighting the role of serum proteins in these kinds of studies involving treatment response (**Priyanka Chandel, et al., 2016**).

In a study done by **Jun Lin et al., (2019**), albumin and globulin in pre and post chemotherapy glioma patients was calculated and the optimal cut- off values of AG ratio was found to be 1.32. It was concluded by the study that the preoperative AGR was correlated with clinical prognosis of patients with high-grade gliomas (HGG), and the survival time of the patients both high AGR (AGR>1.32) was significantly larger. The prognosis of patients with high AGR was better in isocitrate dehydrogenase wild-type HGG.

2. Conclusion

All the studies successfully established that the estimation of AGR is a very useful prognostic marker in cancer patients and can also show the side effects of chemotherapy in these patients. Serum protein analysis is thus a very important cost-effective and efficient tool to monitor cancer patients, to see their response to treatment, to see side-effects of therapy and thus to evaluate the prognosis of cancer patients.

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