



## Evaluation of serum biochemical profile of breast cancer patients

Chauhan P.<sup>1</sup>, Yadav R.<sup>\*1</sup>, Kaushal V.<sup>2</sup> and Beniwal P.<sup>1</sup>

<sup>1</sup>Department of Genetics, M.D. University, Rohtak

<sup>2</sup>Department of Radiotherapy, Pt. B.D. Sharma University of Health Science, Rohtak

\*Correspondance E mail: [ritu.genetics@rediffmail.com](mailto:ritu.genetics@rediffmail.com)

### ABSTRACT

Breast cancer is the most common cancer worldwide. The incidence and mortality rate is increasing in developing countries as compare to developed countries. The aim of this study was to evaluate the effect of different courses of chemotherapy treatment on serum biochemical profile of breast cancer patients. In the present study, two hundred breast cancer patients were selected to study variations in serum biochemical level of breast cancer patients. The mean values of blood urea nitrogen, creatinine, uric acid, aspartate aminotransferase (SGOT), alanine aminotransferase (SGPT) and alkaline phosphatase was found to be  $32.58 \pm 19.7$ mg/dl,  $1.05 \pm 0.59$ mg/dl,  $8.6 \pm 1.3$ mg/dl,  $27.3 \pm 4.02$ U/L,  $27.9 \pm 10.24$ U/L and  $111 \pm 24.04$ U/L before the start of chemotherapy courses. The mean values of total and direct bilirubin, total serum protein, albumin, Fasting and postprandial glucose level was  $0.30 \pm 1.3$ mg/dl,  $0.13 \pm 0.11$ mg/dl,  $8.11 \pm 0.5$ g/dl,  $3.5 \pm 0.07$ g/dl,  $96 \pm 25$  mg/dl and  $110 \pm 25$ mg/dl before the start of chemotherapy treatment. The level of serum blood urea nitrogen, uric acid, alkaline phosphatase, bilirubin and post-prandial glucose level was found to be more than normal reference range; while the level of creatinine, aspartate aminotransferase (AST or SGOT), alanine aminotransferase (ALT or SGPT), total serum protein, albumin and fasting blood glucose level was reported to be within normal reference range during the different courses of chemotherapy. In conclusion, present results suggest serum biochemical parameters as an important diagnostic tool in the disease monitoring and metastasis.

**Keywords:** Breast cancer, Biochemical profile, chemotherapy, prognostic significance

### INTRODUCTION

Breast carcinoma is the most common malignancy and leading cause of death in women worldwide <sup>[1]</sup>. Breast cancer is heterogeneous in its clinical, genetic and biochemical profile. The incidence rate of breast cancer is much lower in Asian countries as compare to western countries. Breast cancer incidence is increasing in all regions of the world with majority of rise seen in developing countries <sup>[2]</sup>. The age-standardized incidence rate for breast cancer in India is one-third that of Western countries <sup>[3]</sup>.

Complete blood count is a prerequisite investigation for breast cancer patients before the use of any treatment <sup>[4]</sup>. The cancer treatments like chemotherapy and radiation therapy generally destroy the cancerous cells in the body. However, some of the normal cells are also sensitive to these treatments and get damage in the process. Some cancer treatments interfere with blood cells production of the body. Complete blood counts are routinely performed during chemotherapy and other breast cancer treatments to check the number of each type of blood cell circulating in the body. The complete blood count also helps to check for different side effects of chemotherapy.

Blood chemistry panel (BCP) is a common tests used to evaluate a variety of chemical components released from body tissues or produced during the breakdown or metabolism of certain substances. The blood chemistry panel (BCP) measures the levels of chemicals, enzymes, and organic waste products found in the blood. It determines the healthiness and proper functioning of various organs during chemotherapy treatment. The abnormal blood chemistry results also suggest the spread of breast cancer to the bone, kidney or liver. Only a few studies have investigated the associations of liver function tests (LFTs) and kidney function tests (KFTs) with mortality in breast cancer <sup>[5, 6]</sup>.

In the present study, the liver functioning (LFT) and kidney functioning (KFT) were assessed to check the level of different components. The liver function tests measured the levels of important chemicals including liver transaminase (SGOT, SGPT), alkaline phosphatase, albumin; bilirubin, serum proteins and blood glucose level [7]. The term kidney function test (KFT) is used for a variety of tests including blood urea nitrogen, creatinine and uric acid in the blood; performed to evaluate the kidneys functioning.

### MATERIALS AND METHODS

The present study was conducted on the two hundred breast cancer patients being treated at Pt. B.D. Sharma University of Health and Sciences (PGIMS), Rohtak, Haryana. Blood analysis of two hundred female breast cancer patients undergoing chemotherapy was performed. All samples were taken after institutional ethical committee permissions and personal consent of the patients or guardians.

The blood samples were collected from the patients; in heparinized tubes. The collected samples were analysed for biochemical profile of blood. The biochemical parameters like blood urea nitrogen (BUN), Creatinine, uric acid; SGOT, SGPT, Alkaline Phosphatase, bilirubin (direct & total), albumin, total serum protein and blood glucose were included in this study. The statistical analyses were done by Microsoft Excel Windows 10.

### RESULTS

In the present study, two hundred breast cancer patients were studied for prognostic significance of peripheral blood. The mean age of breast cancer patients was  $47.49 \pm 10.43$ . Maximum patients were from rural background (66%) with no education (76%).

Biochemical tests were also performed during chemotherapy treatment (from course 1 to course 5). Blood urea nitrogen (BUN) provides a rough measurement of the glomerular filtration rate. During chemotherapy courses the level of blood urea nitrogen (BUN) was observed to be more than normal range (7-20 mg/dl). The mean value of blood urea nitrogen before the start of chemotherapy courses was found to be  $32.58 \pm 19.7$ . Decreasing pattern of blood urea nitrogen level was noted during chemotherapy treatment as non-significant value (Figure 1).

The mean value of creatinine during the chemotherapy treatment of breast cancer patients observed to be within normal reference range (0.6-1.1 mg/dl). The mean value of creatinine was noted to be  $1.05 \pm 0.59$  mg/dl before the start of chemotherapy. No specific alterations were observed in creatinine level during the different courses of chemotherapy (Figure 1).

Uric acid test is used to determine the rapid cell turnover as an effect of chemotherapy. The mean value of uric acid level was observed to be  $8.6 \pm 1.3$  mg/dl before the start of courses of chemotherapy. The uric acid level was reported to be higher than the normal reference range (2.4-6.0 mg/dl) during the different courses of chemotherapy treatment (Figure 1). Increased uric acid level acts as protective agent as it functions as antioxidant.

The level of enzymes (aspartate aminotransferase, alanine aminotransferase, and alkaline phosphatase) and proteins (total serum protein and albumin) were analyzed for the proper functioning of liver. Liver function test was used to screen liver infection, to monitor disease progression and possible side effects of medication used in chemotherapy. The mean value of Aspartate aminotransferase (AST or SGOT) level before the start of chemotherapy treatment was noted to be  $27.3 \pm 4.02$  U/L. The mean value of SGOT level was observed to be within normal reference range (5-40 U/L) from the first course of chemotherapy to the third course of chemotherapy. However, SGOT level increases as the courses of chemotherapy further proceeds (Figure 2).

The mean value of alanine aminotransferase (ALT or SGPT) level was reported to be within normal reference range (7-56 U/L) during the five courses of chemotherapy treatment. The mean value was noted to be  $27.9 \pm 10.24$  U/L before the start of treatment. An increasing level of SGPT enzyme was reported during the treatment courses (Figure 2). Increased SGPT level indicate the improper liver functioning.

The mean value of alkaline phosphatase in pre chemotherapy state was  $111 \pm 24.04$  U/L. The level of alkaline phosphatase from chemotherapy course 1 to course 4 was observed to be within in normal range (44-147 IU/L), but slightly increased at the level of fifth cycle of chemotherapy (Figure 2). Increased value provides the evidences of liver and bone damage.

The two forms of bilirubin were measured to determine the conditions such as liver disease, hemolytic anemia, and blockage of the bile ducts during the different courses of chemotherapy. The total bilirubin level was observed to be

increased as treatment proceeded from first course to fifth course chemotherapy (Figure 3). The mean value of total bilirubin was  $0.30 \pm 1.3$  mg/dl before the starting of the treatment. Elevated bilirubin level may be a result of hemolytic or pernicious anemia, transfusion reaction, viral hepatitis or drug reaction. The mean value of direct bilirubin was  $0.13 \pm 0.11$  mg/dl before the starting of the treatment. Direct bilirubin level was found to be increased after the fourth cycle of chemotherapy (Figure 3).

In serum protein profile, the level of albumin and total proteins was measured to determine the proper liver and kidney functioning. In the present study, a decreased level of albumin was observed in breast cancer patients undergoing chemotherapy treatment (Figure 4). This decline may be due to increased generation of reactive oxygen species and free radicals.

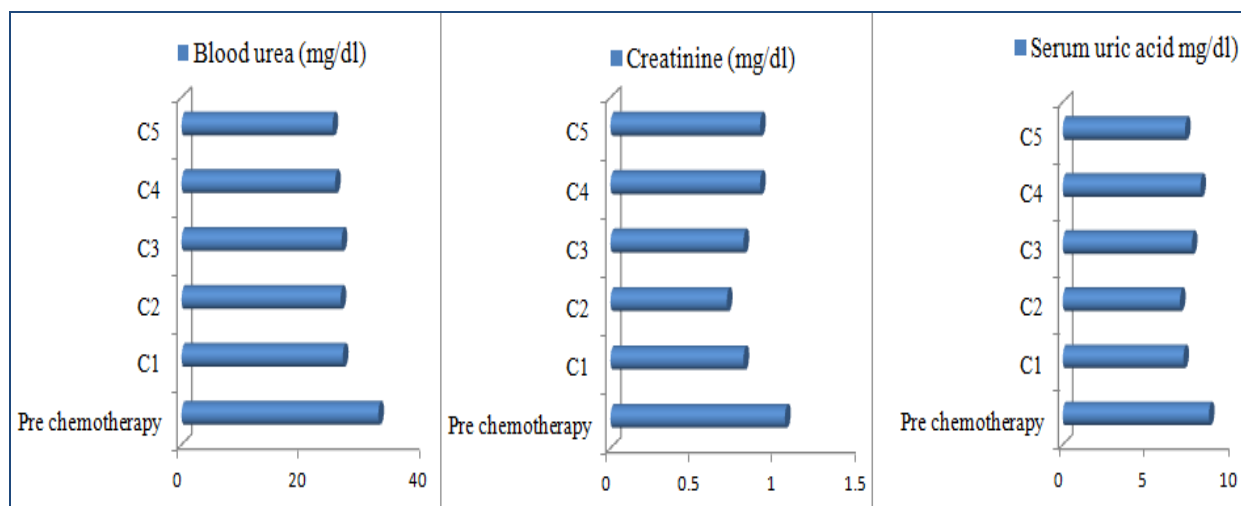


Figure 1: Variations of blood urea, creatinine and uric acid count of breast cancer patients during five courses of chemotherapy

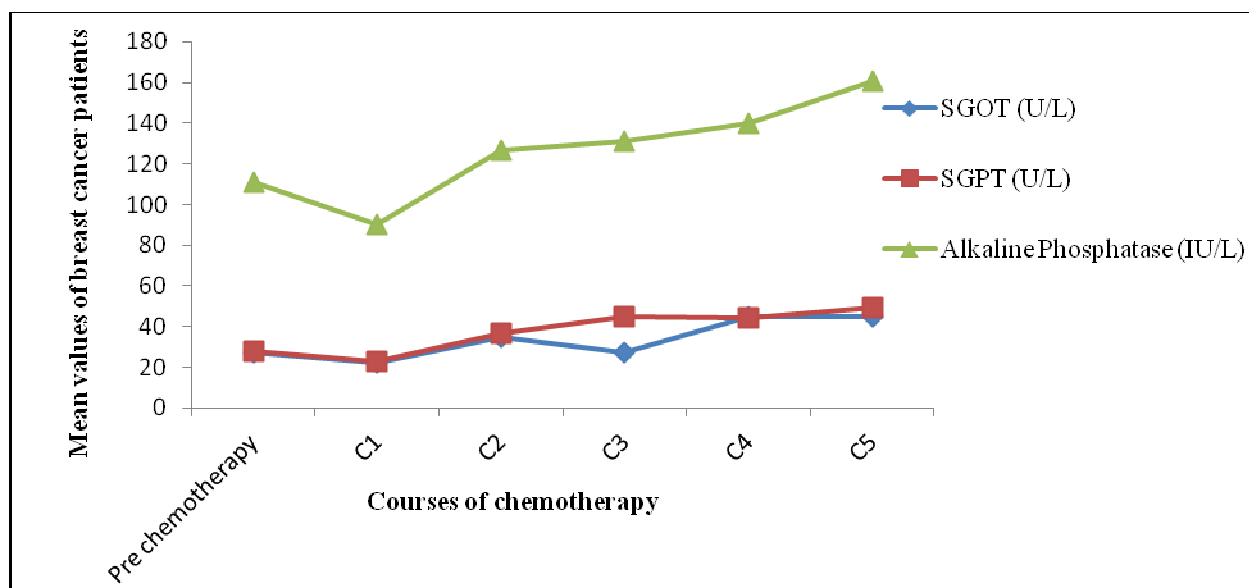


Figure 2: Variations of SGOT, SGPT and alkaline phosphatase of breast cancer patients during five courses of chemotherapy

The mean value of albumin was noted to be  $3.5 \pm 0.07$  g/dl. During the treatment courses of chemotherapy; albumin level was within normal range (3.5-5.5g/dl).The total serum protein was found with non-significant decreased level during the different courses of chemotherapy (Figure 4). The mean value of total serum protein was observed to be  $8.11 \pm 0.5$  g/dl before chemotherapy. The level was found within normal range (6-8.3g/dl).

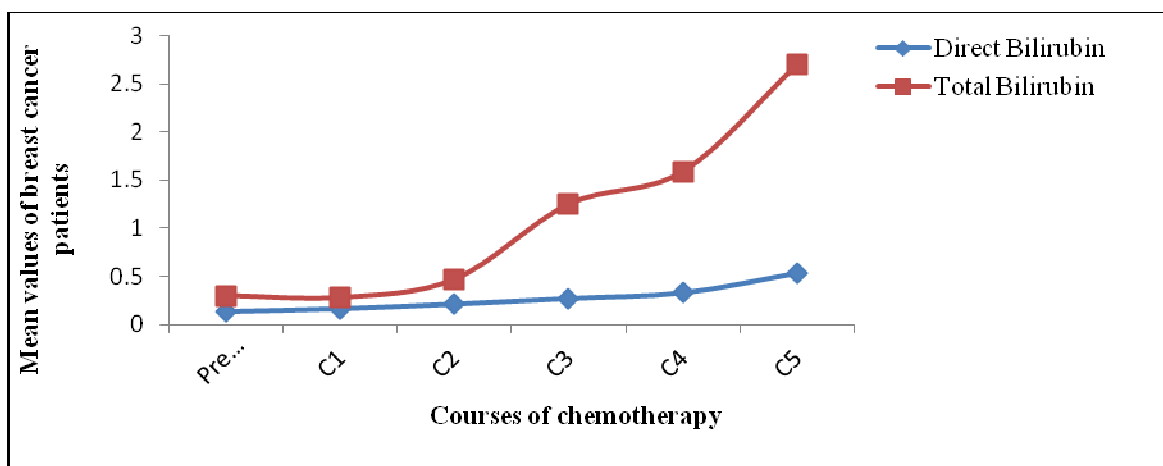


Figure 3: Variations of blood total and direct bilirubin count of breast cancer patients during five courses of chemotherapy

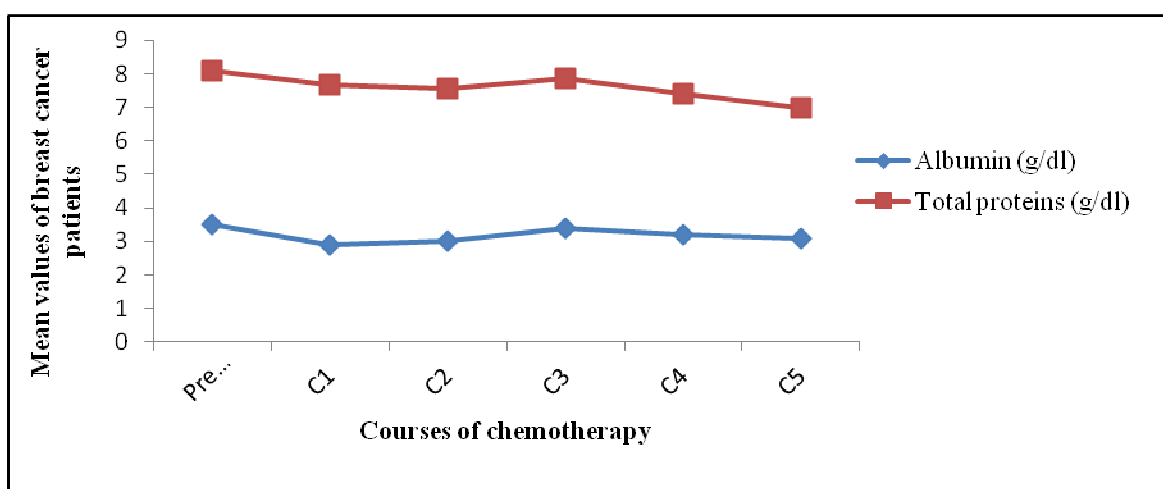


Figure 4: Variations of serum proteins of breast cancer patients during five courses of chemotherapy

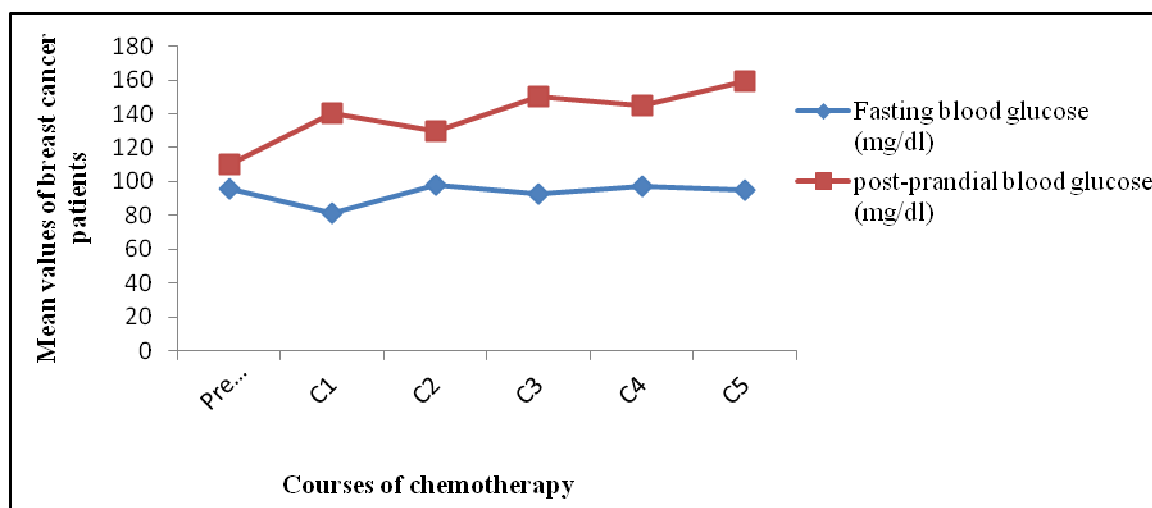


Figure 5: Distribution of blood glucose level in breast cancer patients during five courses of chemotherapy

The blood glucose level was counted pre-prandial (before eating) also known as fasting blood sugar (FBS) and post prandial (1-2 hour after eating). No appreciable change was observed in fasting blood sugar level during different courses of chemotherapy. The mean value of FBS was reported to be  $96 \pm 25$  mg/dl before chemotherapy. The FBS level was found within normal reference range (70-108 mg/dl). Post-prandial glucose level showed a slight increased level during different courses of chemotherapy. The mean value of post-prandial glucose level was noted to be  $110 \pm 25$  mg/dl before chemotherapy. In post-prandial glucose level, the mean values were greater than normal

range (100-140 mg/dl). Elevated glucose level can lead to certain serious conditions like kidney failure, heart attacks, vision loss, weakened immune system and slow wound healing (Figure 5).

## DISCUSSION

Biochemistry profiles of blood measure the chemical substances released from body tissues or are produced during the breakdown (metabolism) of certain substances. The analysis of blood chemistry provides important information about the function of the kidneys, liver and other organs. In the present study, the liver functioning (LFT) and kidney functioning (KFT) were assessed to check the level of different components.

Blood urea nitrogen (BUN) is a sensitive indicator of renal abnormalities. In the present study, BUN level was reported to be more than normal reference range in contrast to other studies<sup>[8]</sup>. Devi et al. (2015) observed the waste metabolite levels slightly increase and decrease were mostly within the normal range. Urea (BUN) concentration was in normal range in patients.

The level of creatinine in serum is considered more sensitive kidney function test than BUN. As kidney impairment is the only cause of elevated creatinine. In this study, no statistically significant association was found in creatinine during different courses of chemotherapy in contrast to other studies [8]. Devi et al. (2015) observed the increased value of creatinine level ranges between 1.0 and 2.0mg/dl.

There are many studies on the correlation between serum uric acid and outcomes of breast cancer patients<sup>[9, 10]</sup>. Many studies have found that the high level of serum uric acid is associated with a variety of disorders mainly renal insufficiency<sup>[9, 11]</sup>. Uric acid acts as pro-oxidant and marker of oxidative stress, it plays a therapeutic role as an antioxidant<sup>[12,13]</sup>. In present study, serum uric acid level decreased and then slightly increased during different courses of chemotherapy; similar to other studies<sup>[14,15]</sup>. These studies showed that increased uric acid level may be a protective agent<sup>[16,17]</sup>. Veni et al. (2011) observed a significant rise in uric acid level in untreated women of breast cancer patients, which may be due to high oxidative stress. In the present study, uric acid level is found to be higher than the normal range similar to the other studies<sup>[18]</sup>.

Liver dysfunction associated with an overload of hepatotoxins or hepatotoxicants is known as hepatotoxicity<sup>[19]</sup>. Hepatotoxicity enhances necrosis, steatosis, fibrosis, cholestasis, and vascular injury<sup>[20]</sup>. Liver functioning test (LFT) is mainly based on enzymatic level of SGOT, SGPT and alkaline phosphatase.

Serum glutamate oxaloacetate transaminase (SGOT) and serum glutamate pyruvate transaminase (SGPT) catalyze the aspartate into oxaloacetate and alanine into pyruvate, respectively. Some studies have established that malignant breast cancer patients have increased activities of these transaminases than in benign breast cancer patients<sup>[21,22]</sup>. The elevation in SGOT and SGPT suggests impairment in liver and kidney function which could be caused by tumor invasion<sup>[22]</sup>. In the present study, the level of alkaline phosphatase was higher than the normal range while the levels SGOT, SGPT were within the normal range. The mean value of SGOT and SGPT was found to be increased significantly similar to other studies<sup>[8,22,23]</sup>.

The progressive increase in the serum alkaline phosphatase (ALP) activity in breast cancer patients is an indication of metastasis<sup>[24,25]</sup>. In the present study, the increased ALP level was noticed during different chemotherapy courses. This indicates the metastasis of breast cancer either to bone or liver. Some studies didn't find any significant difference in ALP levels in non-metastatic breast cancer<sup>[26,27]</sup>.

The relationship of serum bilirubin level with survival has been evaluated in metastatic breast cancer patients and the results showed that hyperbilirubinemia was associated with worse survival<sup>[5,28]</sup>. However, some study revealed that non-metastatic breast cancer patients with higher total bilirubin levels had better overall survival compared with those with lower bilirubin levels<sup>[29]</sup>. This may be due to the differences in patient population. Serum bilirubin level may have different predictive effect in metastatic and non-metastatic breast cancer patients<sup>[29]</sup>.

In the present study, increased level of bilirubin was observed during chemotherapy treatment process, consistent with other studies<sup>[23]</sup>. Serum bilirubin level in breast carcinoma women were found to be within normal range. The level of bilirubin in normal range may be due to bilirubin scavenger during oxidative load or oxidative stress in breast cancer. Some studies have found non-significant correlation between bilirubin level and different chemotherapy courses<sup>[18]</sup>.

Total human serum protein profile is made up of albumin and globulins<sup>[30]</sup>. In this study, the total protein level was found to be non-significantly reduced during the treatment process, consistent with other studies<sup>[22,31]</sup>.

Many studies have found marked variation in level of different proteins. That's why the level of different proteins should be considered instead of the amount of total proteins<sup>[30]</sup>. This fact is supported by decrease in one type through catabolism (albumin) and increase in the other (globulins) through synthesis, in response to breast cancer to compensate the first which consequently contributes to the serum levels of total proteins<sup>[32]</sup>. This could be the possible mechanism that supports a non-significant change in serum levels of total proteins in this study.

Serum albumin is the most abundant protein, comprising more than half of the blood serum proteins<sup>[33]</sup>. Reduced serum albumin (SA) level is used as an independent prognostic indicator in breast cancer<sup>[32,34,35]</sup>. In this study a marked reduction of serum albumin level was observed during the chemotherapy treatment within normal reference range. This decline of serum albumin is associated with poor survival and increased mortality of the patients regardless of the stage of breast cancer<sup>[31,36,37]</sup>.

The level of glucose plays an important role in breast cancer therapy. Many studies have observed the effect of hyperglycemia on the biological behavior of tumor cells and its treatment<sup>[38]</sup>. Some studies showed that hyperglycemia during chemotherapy for hematologic and solid tumors are correlated with increased toxicity<sup>[39]</sup>. In this study, no appreciable changes were noted in fasting blood glucose level, but a slight increased value was observed for post-prandial glucose level. There is no clear biological explanation for the role of the elevated blood glucose level during breast cancer treatment. An independent role for fasting glucose in carcinogenic processes has been proposed with a variety of potential mechanisms, ranging from the generation of free radicals to the induction of damage to DNA repair enzymes<sup>[40]</sup>. It has been speculated for over half a century that the increased availability of glucose in the blood could encourage the growth of potentially malignant cells which require glucose for progression<sup>[41]</sup>.

## CONCLUSION

The present study focused on evaluation of serum biochemical profile of breast cancer patients undergoing chemotherapy treatment. Chemotherapy treatment may results in increasing or decreasing level of biochemical components of blood and hence affecting organ system. Increased level of bilirubin alkaline phosphatase, blood urea nitrogen and uric acid directly affects the functioning of liver and kidney. The study of serum biochemical parameters may be a helpful diagnostic tool in the monitoring of disease, metastasis and different treatment strategies of breast cancer.

## Acknowledgment

Authors are grateful to acknowledge the M.D. University Rohtak and Health University, Rohtak for providing the help and support.

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