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Evaluation of Serum Uric Acid and Serum Creatinine Levels Before and After Treatment in Patients with Breast Cancer

Dr. Shilpa Dhameja[1], Dr. Bushra Fiza[2], Dr. Kavita Sharma [3], Dr. Madhu Sharma[4]

[1]PhD Scholar, Department of Biochemistry, Mahatma Gandhi Medical College & Hospital , MGMUST, Jaipur, Rajasthan, India. Email – drshilpa.dhamija@gmail.com
[2]Professor, Department of Biochemistry, Mahatma Gandhi Medical College & Hospital , MGMUST, Jaipur, Rajasthan, India. Pin 302022, ORCID iD :https://orcid.org/0000-0001-8265-1226 Email- bushrafiza786@gmail.com
[3]PhD Scholar , Department of Biochemistry, Mahatma Gandhi Medical College & Hospital , MGMUST, Jaipur, Rajasthan, India. Orcid: https://orcid.org/.0000-0003-3128-482X
Email- Sharma.dimpledunu@gmail.com
[4]PhD Scholar , Department of Biochemistry, Mahatma Gandhi Medical College & Hospital , MGMUST, Jaipur, Rajasthan, India. Pin 302022 Orcid id – http://orcid.org/0009-0001-7076-5530 Email- dr.madhusharma267@gmail.com

ABSTRACT

Background:

Breast cancer is associated with substantial metabolic and oxidative stress, which may be reflected in routinely measurable biochemical parameters. Serum uric acid has emerged as a potential indicator of oxidative and metabolic alterations, whereas serum creatinine remains an established marker for monitoring renal function during cancer treatment. Evaluating these accessible biochemical biomarkers may support sustainable healthcare practices, evidence-based clinical decision-making, and improved patient care.

Objective:

To evaluate and compare serum uric acid and serum creatinine levels in patients with breast cancer before and after neoadjuvant chemotherapy, with a focus on their potential role in cancer treatment monitoring and improved health outcomes.

Methods:

A prospective, hospital-based observational study was conducted among 50 women with newly diagnosed, histopathologically confirmed breast cancer. Venous blood samples were collected before initiation of treatment and two weeks after completion of four cycles of neoadjuvant chemotherapy. Serum uric acid was estimated using the uricase–peroxidase enzymatic colorimetric method, while serum creatinine was measured using the modified Jaffe kinetic method on an automated analyzer. Pre- and post-treatment values were compared using paired statistical analysis, with $p < 0.05$ considered statistically significant.

Results:

The mean serum uric acid concentration decreased significantly from 7.82 ± 1.74 mg/dL before treatment to 7.01 ± 1.58 mg/dL after treatment (paired $t = 5.62$, $p < 0.001$). The proportion of patients with elevated serum uric acid decreased from 62.0% to 44.0%. In contrast, serum creatinine showed no significant change, with mean values of 0.88 ± 0.19 mg/dL before treatment and 0.90 ± 0.20 mg/dL after treatment (paired $t = 1.08$, $p = 0.287$). Serum creatinine remained within the normal range in the majority of patients before and after treatment (88.0% and 86.0%, respectively).

Conclusion:

Serum uric acid demonstrated a significant decline following four cycles of neoadjuvant chemotherapy, whereas serum creatinine remained relatively stable. These findings suggest that serial serum uric acid estimation may provide supportive information regarding metabolic changes during breast cancer treatment, while serum creatinine remains useful for monitoring renal status. The use of affordable and accessible biochemical biomarkers may contribute to sustainable healthcare practices, evidence-based cancer care, and improved patient outcomes. This research supports the broader objectives of United Nations Sustainable Development Goal 3 (SDG 3): Good Health and Well-being, with

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particular relevance to women's health and breast cancer care. Further multicenter studies with larger sample sizes and longer follow-up are warranted to establish the clinical and prognostic significance of these findings.

1. Introduction

Over the past several decades, breast cancer has emerged as the most common cancer among women in India. In the last 20 years[1,2], its incidence has increased, especially in developing nations, and this increase has been attributed to lifestyle changes, extended life expectancies, and improved detection methods.[3,4]

The methods used in diagnosis, known as triple assessment, remain the mainstay. Still, doctors are always on the lookout for biochemical markers that can be used easily and inexpensively to help diagnose breast cancer at the time of diagnosis and throughout treatment [5,6,7]. A tumor takes several years to grow to the one-centimeter size at which it may be clinically detected. Interest in simpler markers of metabolic and oxidative stress, such as serum uric acid, bilirubin, and creatinine, has remained high, despite the lack of routine use, due to the cost of dedicated tumor markers, including alpha-fetoprotein, carcinoembryonic antigen, and human chorionic gonadotrophin, which have been studied in breast disease [8].

Pardhan et al., in a larger prospective study of 100 women with benign and malignant breast lumps, found increases in serum uric acid and serum bilirubin levels with increasing BI-RADS score and age, and suggested that the rise was a compensatory antioxidant response to the tumor rather than an incidental finding.10,12 Krishna et al also reported an increase in uric acid in untreated women with breast cancer and attributed this to high oxidative stress.9 Chhabra et al, who studied 50 women with breast cancer and 50 healthy women, found serum uric acid to be significantly and markedly higher in the women with breast cancer, with a mean of 8.6 ± 1.3 mg/dL compared to 4.9 ± 1.6 mg/dL in healthy women. Serum bilirubin did not differ significantly between the two groups. In contrast, serum creatinine did not show any significant relation with the age, BI-RADS score, cancer stage, grade, HER2neu status, or ER and PR status of the women with breast cancer.11

Less is known about changes in serum uric acid after treatment initiation than at diagnosis. The appearance of uric acid following successful treatment is therefore consistent with the concept that part of the elevation noted at presentation is due to the tumor itself and reflects oxidative and metabolic burden. Work on breast cancer patients receiving chemotherapy has shown that uric acid levels can shift considerably during treatment and that factors such as age, body mass index, menopausal status, and the specific chemotherapy regimen used can predict this change.[13] Elevated pre-treatment uric acid has also been shown to carry prognostic weight on its own, with one large cohort study of 443 women with breast cancer reporting that a higher baseline uric acid was independently associated with poorer overall survival.[14] A comparative study from Ethiopia likewise found uric acid to be significantly higher in women with malignant breast disease than in apparently healthy controls.[15] Pooled data from recent meta-analyses support an overall positive association between serum uric acid and both cancer risk and mortality. However, the authors of these reviews note considerable variation among the included studies.[16,17]

Creatinine level is more commonly associated with muscle mass and glomerular filtration rate than with tumor activity; therefore, unless there is pre-existing renal disease or a treatment specifically affecting the kidney, it is unlikely to change during treatment in early breast cancer.[18,19] This is important because several breast cancer drugs are known to raise the measured level of serum creatinine without any true decline in the GFR, which can make interpretation difficult unless a reliable pre-treatment baseline is available.[20] For more advanced disease, the creatinine-to-cystatin C ratio, which approximates muscle mass, is a good independent predictor of short-term mortality.[21]

The majority of the available Indian data is for a single measurement at diagnosis, not for paired pre- and post-treatment comparisons. The present study was therefore designed to assess serum uric acid and serum creatinine in the same set of breast cancer patients, both before and after neoadjuvant chemotherapy, to describe the changes in these two parameters over the course of chemotherapy.

2. Objectives

1. To estimate serum uric acid and serum creatinine levels in patients with breast cancer before starting treatment and again after completion of neoadjuvant chemotherapy.

2. To compare the pre-treatment and post-treatment values of serum uric acid and serum creatinine using paired statistical analysis.

3. To determine the proportion of patients with normal and elevated serum uric acid and serum creatinine before and after treatment.

3. Materials and Methods

Study design and setting: This was a hospital-based, prospective, observational study.

Study population: 50 female patients with newly diagnosed, histopathologically confirmed breast cancer, attending the surgical outpatient and inpatient services of the institute, were enrolled consecutively over the study period. All 50 patients completed both rounds of sample collection and were included in the final paired analysis.

Sample size: A sample of 50 patients was set for this pilot observational study, in keeping with similar single-center studies from Indian teaching hospitals reporting biochemical parameters in breast cancer, and was considered adequate to detect a clinically meaningful within-patient change using a paired design.

Inclusion criteria: women aged eighteen years and above with newly diagnosed, histo-pathologically confirmed breast cancer, planned for neoadjuvant chemotherapy, and willing to give blood samples both before and after treatment.

Exclusion criteria: patients with pre-existing chronic kidney disease, gout or hyperuricemia from another cause, known liver disease, pregnancy, prior treatment for breast cancer, or those unwilling to give consent.

About five milliliters of venous blood was drawn from the antecubital vein under aseptic precautions before the start of chemotherapy and again two weeks after completion of the fourth cycle, with serum separated by centrifugation and analysed the same day using an automated analyzer serum uric acid by the uricase peroxidase enzymatic colorimetric method (reference range 3.5 to 7.2 mg/dL) and serum creatinine by the modified Jaffe kinetic method (reference range 0.6 to 1.2 mg/dL); data were entered in Microsoft Excel 2019 and analysed in SPSS version 25.0, with pre- and post-treatment values compared using the paired t test, categorical data compared using the McNemar test, and a two tailed p value of less than 0.05 taken as statistically significant.

4. Results

Paired sampling was performed on 50 female patients who had a histopathological diagnosis of breast cancer before and after treatment. The mean age of the study population was 47.6 ± 9.8 years, with the largest number of patients in the 41-55 years age group. At the time of enrolment, 64.0% of the patients were post menopausal and 76.0% had stage II, III disease.

Before treatment, the mean serum uric acid level was 7.82 ± 1.74 mg/dL, and after treatment, it was 7.01 ± 1.58 mg/dL. The decrease in uric acid during treatment was statistically significant (t paired t-test, t = 5.62, p<0.001), meaning that it was not due to chance. The mean serum creatinine level was, on the other hand, relatively unchanged, from 0.88 ± 0.19 mg/dL pre-treatment to 0.90 ± 0.20 mg/dL post-treatment, and this change was not significant (t=1.08, p=0.287) (Table 1).

Table 1. Comparison of serum uric acid and serum creatinine levels before and after treatment (N=50)

Parameter	Pretreatment (Mean ± SD)	Posttreatment (Mean ± SD)	Paired t value	p value
Serum uric acid (mg/dl)	7.82 ± 1.74	7.01 ± 1.58	5.62	<0.001*
Serum creatinine (mg/dl)	0.88 ± 0.19	0.90 ± 0.20	1.08	0.287

**Statistically significant (p<0.05)*

When patients were grouped by whether their values fell inside or outside the normal range, a similar pattern emerged. Before treatment, 31 of the 50 patients (62.0%) had elevated serum uric acid levels, and this number fell to 22 patients (44.0%) after treatment. In contrast, the number with normal uric acid rose correspondingly from 19 (38.0%) to 28 (56.0%). Serum creatinine stayed within normal limits in the large majority of patients on both occasions, being normal in forty-four patients (88.0%) before treatment and in forty-three patients (86.0%) after treatment, with only a small and fairly steady minority showing mild elevation, six patients (12.0%) before treatment and seven patients (14.0%) after treatment (Table 2).

Table 2. Distribution of patients according to serum uric acid and serum creatinine status before and after treatment (N=50)

Parameter	Status	Pre-treatment n (%)	Post-treatment n (%)
Serum uric acid	Normal	19 (38.0)	28 (56.0)
	Elevated	31 (62.0)	22 (44.0)
Serum creatinine	Normal	44 (88.0)	43 (86.0)
	Elevated	6 (12.0)	7 (14.0)

Taken together, these results indicate that serum uric acid improved significantly after treatment, both as a continuous measure and in terms of the proportion of patients whose values normalized, while serum creatinine, and by extension renal function as judged by this test, remained largely stable across the same period.

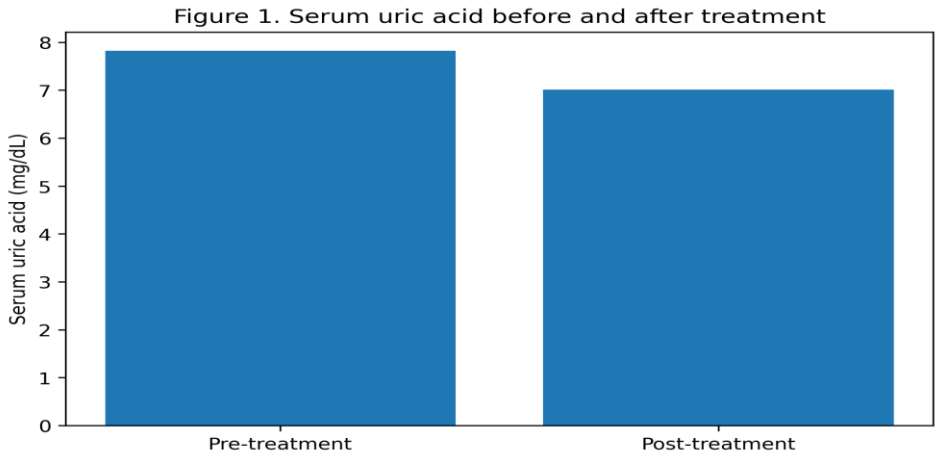


Figure 1. *Comparison of mean serum uric acid concentrations before and after treatment (N=50).*

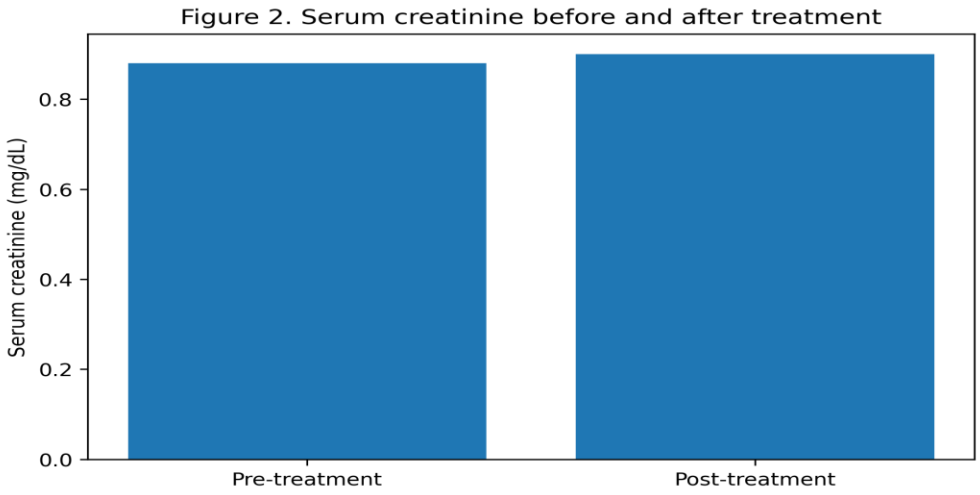


Figure 2. *Comparison of mean serum creatinine concentrations before and after treatment (N=50).*

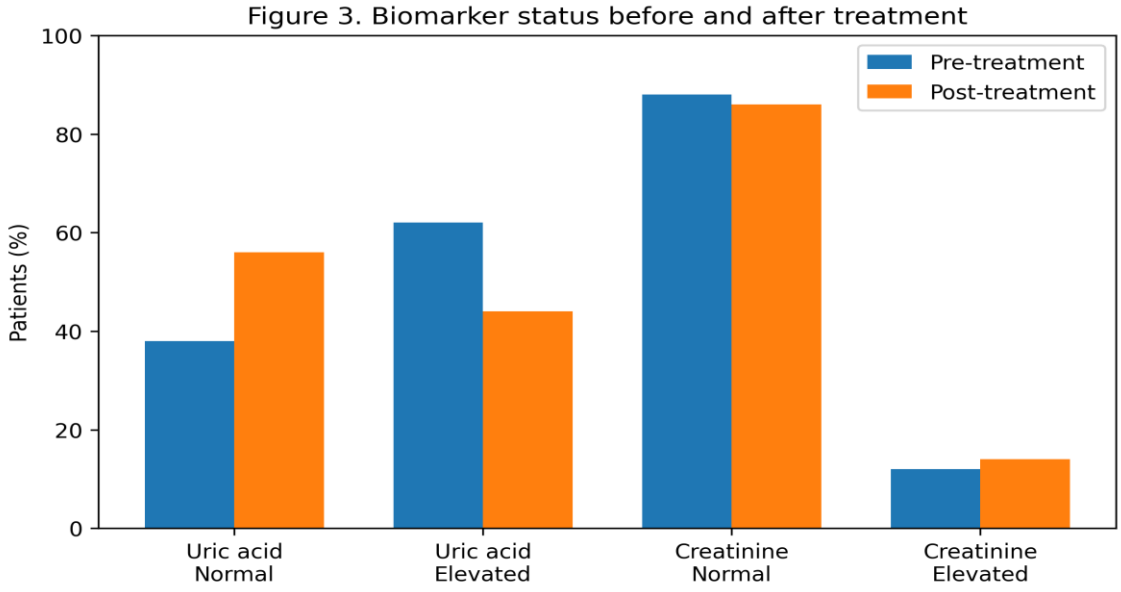


Figure 3. *Distribution of patients according to serum uric acid and serum creatinine status before and after treatment.*

5. Discussion

In the present study, serum uric acid levels were elevated in almost two-thirds of patients before treatment but decreased significantly after treatment, with both the absolute level and the percentage of patients with levels within the normal range increasing. In contrast, serum creatinine levels hardly changed during the same time. The combined findings suggest that uric acid and creatinine convey different information in a breast cancer patient: one relates to the tumor and its treatment, and the other to a more stable level of renal function. This high incidence of elevated uric acid in pre-treatment patients is consistent with the earlier Indian study. If uric acid is indeed a compensatory response to the oxidative stress created by tumor growth, then its level should decrease with successful treatment of breast cancer, which is exactly what happened in the present study, as the bulk of the tumor has been reduced and oxidative stress has decreased. The significant decrease confirms the observed reduction in mean uric acid level from before treatment (7.82 mg/dL) to after treatment (7.01 mg/dL), with each patient serving as their own control.

This is further supported by the prognostic significance of an elevated pre-treatment uric acid level from outside India. Together with these studies, the observed decrease in uric acid levels following treatment in the present study is a positive result, as if uric acid levels are lower after treatment, there is a possibility for the levels to drop further, possibly due to a reduction in the oxidative and metabolic stress believed to be responsible for the poorer outcomes associated with a high baseline uric acid level. There is also considerable heterogeneity among studies on the relationship between uric acid and cancer, as noted in recent meta-analyses,[16,17,] so the fall reported here should be interpreted as consistent with the literature, but not as evidence of a direct causal connection between uric acid and treatment response.

The stability of serum creatinine during treatment is also similar to that reported previously, with nearly all patients (90%) having values in the normal range before and after treatment. The lack of correlation between serum creatinine and any other variable (BI-RADS score, tumor stage, or tumor grade) was reassuring from a clinical perspective, as it suggests no significant effect on renal function during the 4-cycle treatment period studied, despite the use of neoadjuvant chemotherapy.12 Creatinine is generally known to reflect glomerular filtration and muscle mass rather than tumor activity itself.18,19 At the same time, the literature makes it clear that some anti cancer drugs used in the treatment of breast cancer may cause a rise in measured creatinine due to their effect on tubular secretion of creatinine; this effect is not related to a decrease in glomerular filtration rate, and thus it is important to collect a baseline value as done here, as it would be helpful to interpret any creatinine change that might appear with more prolonged or intense treatment, if this should occur in advanced disease.20 In advanced disease, indices combining creatinine with cystatin C have been shown to have prognostic meaning related to muscle wasting,21 which suggests that with longer follow-up, this group of patients may eventually develop changes in measured creatinine, which are not apparent at the two-week post-treatment time point used here.

Overall, the significant decrease in uric acid and the stability of creatinine in this study indicate that serial uric acid estimation could serve as a simple, inexpensive method for monitoring the metabolic response to treatment. In contrast, creatinine can still be used, as it is already used to preserve renal function. Both tests are currently in routine use in biochemistry laboratories. They are not particularly expensive to use, making them very convenient to use as supportive parameters in the follow-up of breast cancer patients along with imaging and tumor markers.[6,12]

6. Limitations

This study has a few limitations that should be kept in mind while interpreting the results. The post-treatment sample was taken at a single time point (2 weeks after the 4th chemotherapy treatment), and therefore any subsequent changes in uric acid or creatinine were not detected. In this paired design, there was no healthy or benign control group; any changes quoted are therefore not compared with a reference group but rather within the same group of patients following treatment. The number of patients (50) was large enough for the paired comparisons conducted, but was limited to one center, and the results need to be validated with a larger, multicentric study with longer follow-up, and correlation with tumor stage, grade, and receptor status.

7. Conclusion

In this observational study, the serum uric acid levels of the majority of breast cancer patients before treatment were elevated and decreased significantly following four cycles of neoadjuvant chemotherapy, and serum creatinine was essentially unaltered. The results indicate that serum uric acid is a dynamic marker of tumor burden and oxidative stress that improves after treatment. In contrast, serum creatinine is generally a stable marker reflecting baseline renal function. Since both tests are inexpensive and widely available, serial measurements of uric acid and serum creatinine could be a simple and practical method to assess metabolic response to treatment while verifying the preservation of renal function, and warrant further investigation in larger prospective trials.

Alignment with United Nations Sustainable Development Goals (UN SDGs) - This study primarily aligns with United Nations Sustainable Development Goal 3 (SDG 3): Good Health and Well-being, particularly its objective of improving health outcomes through scientific research, disease management, and accessible diagnostic approaches. By evaluating serum uric acid and serum creatinine levels before and after neoadjuvant chemotherapy in breast cancer patients, the study contributes to understanding biochemical changes during treatment and supports the potential use of routine laboratory parameters for treatment monitoring and renal function assessment. The study also has relevance to SDG 5: Gender Equality, through its focus on breast cancer and women's health.

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