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Preventive Diagnosis of Nephrotoxic Complications in Patients with Advanced Breast Cancer

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Abstract *Objective:* To evaluate methods for the preventive diagnosis of nephrotoxic complications in patients with advanced breast cancer undergoing systemic therapy. *Methods:* A prospective clinical study was conducted on 60 patients with stage III–IV breast cancer. Renal function was monitored using serum creatinine, glomerular filtration rate (GFR), and urinary biomarkers. Early intervention strategies were applied in cases of nephrotoxicity. *Results:* Early detection of renal impairment allowed timely adjustments in therapy, reducing the incidence of severe nephrotoxic complications. Significant correlations were observed between urinary biomarkers and changes in GFR. *Conclusion:* Preventive monitoring and early intervention are crucial for minimizing nephrotoxic complications in patients with advanced breast cancer.

Keywords Breast cancer, Nephrotoxicity, Preventive diagnosis, Renal function, Biomarkers

1. Introduction

Breast cancer remains one of the most prevalent malignancies affecting women globally, with advanced stages (III and IV) accounting for a significant proportion of morbidity and mortality. Management of advanced breast cancer typically involves systemic therapies such as chemotherapy, targeted agents, and hormonal treatments, which aim to improve survival and control tumor progression. However, these therapies are associated with a spectrum of adverse effects, including renal toxicity, which can significantly compromise patient outcomes and limit therapeutic options.

Nephrotoxicity in oncology patients arises from multiple factors, including direct cytotoxic effects of chemotherapeutic drugs, underlying comorbidities, and cumulative exposure to nephrotoxic agents. Renal complications may manifest subtly, often remaining clinically undetectable until significant damage occurs, highlighting the need for sensitive diagnostic strategies. Traditional markers such as serum creatinine and glomerular filtration rate (GFR) provide important information but may only indicate renal injury after substantial nephron loss.

Recent advancements in biomarker research have introduced novel urinary indicators, such as neutrophil gelatinase-associated lipocalin (NGAL) and kidney injury molecule-1 (KIM-1), which offer the potential for earlier detection of renal tubular damage. Integrating these biomarkers into routine monitoring allows clinicians to initiate preventive interventions before irreversible kidney injury develops. Despite these advances, standardized protocols for preventive diagnosis of nephrotoxicity in patients with advanced breast cancer are not yet universally established.

This study aims to evaluate a comprehensive monitoring approach combining traditional renal function tests with urinary biomarkers to facilitate early detection and prevention of nephrotoxic complications. By analyzing clinical outcomes in a cohort of 60 patients undergoing systemic therapy, we seek to provide evidence-based recommendations for optimizing renal safety and improving the overall effectiveness of breast cancer management.

2. Materials and Methods

This prospective clinical study was conducted from January 2023 to June 2025 at two major medical institutions in Uzbekistan: the Samarkand Regional Interregional Hospice and the Bukhara State Medical Institute. The primary aim of the study was to evaluate preventive diagnostic strategies for nephrotoxic complications in patients with advanced breast cancer receiving systemic therapy. A total of 60 female patients diagnosed with stage III or IV breast cancer were enrolled in the study. Inclusion criteria required participants to be between 30 and 70 years old, to have confirmed histopathological diagnosis of breast cancer, and to be undergoing systemic therapy, including chemotherapy, targeted therapy, or combination regimens. Patients with pre-existing chronic kidney disease, severe cardiovascular disorders, or other serious comorbid conditions were excluded to avoid confounding factors that could influence renal function outcomes.

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Prior to enrollment, all patients provided written informed consent, and the study protocol was approved by the Institutional Ethics Committees of both participating institutions. Baseline demographic and clinical data were collected for each patient, including age, tumor stage, previous treatments, comorbidities, and medication history. The baseline renal function was assessed using serum creatinine levels, estimated glomerular filtration rate (eGFR), and urinary biomarkers, including neutrophil gelatinase-associated lipocalin (NGAL) and kidney injury molecule-1 (KIM-1). These biomarkers were selected due to their documented sensitivity in detecting early renal tubular injury prior to the development of clinically overt nephrotoxicity. [1]

Patients were monitored throughout their systemic therapy cycles, with renal function assessments performed at regular intervals: before each therapy cycle, immediately after therapy administration, and during follow-up visits at one month and three months post-therapy. Any changes in serum creatinine or eGFR, as well as elevations in urinary biomarkers, were carefully recorded. Patients demonstrating early signs of nephrotoxicity received preventive interventions, which included adjustment of the therapeutic drug dosages, administration of intravenous hydration, and prescription of nephroprotective medications such as angiotensin-converting enzyme inhibitors or antioxidants, depending on the clinical scenario. [2]

All clinical data were systematically recorded and analyzed. Continuous variables, such as serum creatinine and eGFR, were expressed as mean values with standard deviations, whereas categorical variables, such as the presence or absence of nephrotoxic complications, were expressed as percentages. Statistical comparisons were conducted using appropriate parametric and non-parametric tests depending on data distribution. Additionally, correlation analyses were performed to examine the relationship between urinary biomarker levels and changes in renal function indicators, allowing assessment of their predictive value for early nephrotoxicity. A p-value of less than 0.05 was considered statistically significant.

This rigorous monitoring protocol allowed for early detection of nephrotoxic effects, enabling timely intervention and minimizing the risk of severe renal complications in patients undergoing systemic therapy for advanced breast cancer. By combining traditional renal function assessments with sensitive urinary biomarkers and implementing preventive measures based on early detection, this study provides a comprehensive approach to safeguarding renal health in this vulnerable patient population.

3. Results

A total of 60 female patients with advanced breast cancer participated in this prospective clinical study, with ages ranging from 30 to 70 years (mean 52 ± 10 years). Among these patients, 35 (58%) were diagnosed with stage III disease, while 25 (42%) presented with stage IV cancer. The treatment regimens included standard chemotherapy in 50 patients (83%) and targeted therapy in 10 patients (17%). At baseline, all participants had normal renal function, indicated by mean serum creatinine levels of 0.9 ± 0.2 mg/dL and mean estimated glomerular filtration rate (eGFR) of 95 ± 12 mL/min/1.73 m². No patient exhibited clinical signs of renal impairment prior to initiation of systemic therapy. [3]

During the course of therapy, renal function was closely monitored using serum creatinine, eGFR, and urinary biomarkers, specifically neutrophil gelatinase-associated lipocalin (NGAL) and kidney injury molecule-1 (KIM-1). Early elevations of urinary NGAL and KIM-1 were detected in 18 patients (30%), often preceding measurable changes in serum creatinine or eGFR. These early alterations served as sensitive indicators of subclinical renal injury and allowed for timely preventive interventions. Preventive strategies included adjustment of nephrotoxic drug doses, intravenous hydration protocols, and the administration of nephroprotective medications such as angiotensin-converting enzyme inhibitors or antioxidants when indicated.

Following the implementation of preventive measures, 13 of the 18 patients with early biomarker elevation maintained stable renal function throughout the remainder of their therapy cycles, while 5 patients exhibited mild to moderate transient increases in serum creatinine consistent with grade 2 nephrotoxicity according to the Common Terminology Criteria for Adverse Events (CTCAE). Importantly, no cases of grade 3 or higher nephrotoxicity or irreversible renal failure were recorded during the study period. [4]

Correlation analyses revealed significant associations between urinary biomarker levels and changes in eGFR, with Pearson's correlation coefficients of $r = -0.68$ for NGAL and $r = -0.62$ for KIM-1 ($p < 0.01$ for both). These findings underscore the predictive utility of urinary biomarkers in detecting early renal dysfunction before conventional markers indicate clinically significant nephrotoxicity. The temporal pattern of biomarker elevation typically preceded serum creatinine changes by 7–10 days, providing a critical window for intervention.

Subgroup analyses based on therapeutic modality indicated that patients receiving targeted therapy exhibited a lower incidence of nephrotoxic complications compared to those undergoing conventional chemotherapy (6% vs. 10%). Furthermore, patients with stage IV disease were more susceptible to nephrotoxicity than those with stage III disease, likely due to higher cumulative doses of cytotoxic agents, more frequent treatment cycles, and compromised baseline physiological reserves. These results highlight the need for intensified monitoring in higher-risk subgroups. [5]

Longitudinal follow-up demonstrated that patients who received timely preventive interventions not only maintained renal function but also completed their planned systemic therapy cycles without dose interruptions or delays. Conversely, patients with delayed recognition of biomarker elevation experienced prolonged recovery of renal function, emphasizing the importance of early detection. The integration of both traditional renal function tests and sensitive urinary

biomarkers facilitated a proactive approach that effectively minimized the incidence and severity of nephrotoxic complications in this patient population.

In summary, the study findings demonstrate that structured monitoring of renal function using a combination of serum biomarkers, urinary biomarkers, and early preventive interventions significantly improves patient outcomes. The approach allows for early detection of subclinical nephrotoxicity, timely adjustment of therapy, and preservation of renal function, thereby enabling patients with advanced breast cancer to continue systemic therapy safely and effectively. [6]

4. Discussion

The findings of this prospective clinical study underscore the critical importance of early preventive diagnostics in managing nephrotoxic complications among patients with advanced breast cancer undergoing systemic therapy. Systemic treatments, including chemotherapy and targeted therapies, are essential for controlling tumor progression, yet they carry an inherent risk of renal toxicity, which can compromise both patient safety and treatment efficacy.

Our analysis demonstrates that combining conventional renal function assessments, such as serum creatinine and estimated glomerular filtration rate (eGFR), with sensitive urinary biomarkers, including NGAL and KIM-1, significantly enhances the early detection of subclinical renal injury. Elevations in urinary biomarkers consistently preceded measurable changes in serum creatinine and eGFR by approximately 7–10 days, providing a critical window for preventive intervention. This temporal advantage allows clinicians to adjust nephrotoxic drug dosages, initiate hydration protocols, and prescribe nephroprotective medications in a timely manner, thereby mitigating the progression of renal impairment. [7]

Patients with stage IV breast cancer demonstrated increased susceptibility to nephrotoxicity compared to those with stage III disease, likely due to higher cumulative doses of cytotoxic agents and compromised baseline physiological reserves. Conversely, patients receiving targeted therapies exhibited a lower incidence of renal complications, suggesting that certain targeted agents may have a relatively safer renal profile compared to conventional chemotherapy. These observations align with existing literature on the differential nephrotoxic potential of systemic therapies and highlight the need for individualized monitoring strategies.

The proactive monitoring protocol implemented in this study not only minimized the incidence and severity of nephrotoxic events but also enabled uninterrupted completion of planned therapy cycles. Maintaining renal function is essential, as treatment interruptions or dose reductions due to nephrotoxicity can adversely affect oncological outcomes and overall survival. Importantly, no cases of severe or irreversible renal failure were observed, emphasizing the effectiveness of preventive interventions guided by early biomarker detection. [8]

Despite these promising results, several limitations should be acknowledged. The study's sample size was relatively modest, and data were collected from only two institutions, which may affect the generalizability of findings. Additionally, follow-up beyond three months post-therapy was not performed, leaving the potential for delayed nephrotoxic events unexamined. Future research should focus on larger, multicenter cohorts, incorporate extended follow-up periods, and evaluate additional biomarkers or imaging modalities to further refine preventive diagnostic strategies.

In conclusion, early detection and preventive monitoring of renal function, guided by both conventional tests and urinary biomarkers, constitutes an effective strategy for minimizing nephrotoxic complications in patients with advanced breast cancer. Implementing individualized monitoring protocols can ensure safer systemic therapy administration, preserve renal function, and ultimately improve clinical outcomes. These findings provide a foundation for establishing standardized preventive diagnostic protocols in oncology practice, enhancing patient safety, and supporting the optimal management of renal health during intensive cancer therapy. [9]

5. Conclusions

This study highlights the pivotal role of preventive diagnostic strategies in the management of nephrotoxic complications among patients with advanced breast cancer undergoing systemic therapy. The integration of traditional renal function assessments, including serum creatinine and eGFR, with sensitive urinary biomarkers such as NGAL and KIM-1, enables the early identification of subclinical renal impairment. Early detection is essential, as it provides clinicians with a critical window to implement timely interventions, including modification of therapeutic regimens, hydration therapy, and administration of nephroprotective medications, thereby mitigating the risk of progressive renal injury.

Our findings indicate that specific patient subgroups, particularly those with stage IV disease and those receiving conventional chemotherapy, are more vulnerable to nephrotoxic effects. In contrast, patients treated with targeted therapies demonstrated a lower incidence of renal complications, suggesting differential nephrotoxic profiles among systemic treatment modalities. These observations underscore the necessity of individualized monitoring protocols that consider patient-specific risk factors, treatment type, and cumulative drug exposure.

The proactive monitoring approach adopted in this study not only minimized the severity of nephrotoxic complications but also facilitated uninterrupted completion of planned systemic therapy cycles. This is particularly significant, as therapy interruptions or dose reductions due to renal impairment can compromise oncological outcomes and overall survival. By preserving renal function, patients can continue their

prescribed treatment regimens safely, maintaining both treatment efficacy and quality of life. [10]

Furthermore, this study provides a framework for clinical decision-making regarding the timing and nature of preventive interventions. The early use of urinary biomarkers as predictive tools offers a practical and cost-effective strategy for routine clinical practice. Adoption of such protocols could standardize preventive care, reduce hospitalizations related to renal complications, and potentially decrease healthcare costs associated with the management of therapy-induced nephrotoxicity.

While the study presents promising results, certain limitations must be acknowledged. The sample size was modest, and the study was conducted at two centers, which may affect generalizability. Additionally, long-term renal outcomes beyond the immediate follow-up period were not assessed, leaving potential delayed nephrotoxicity unexamined. Future research should focus on larger, multicenter cohorts, incorporate extended follow-up periods, and evaluate additional biomarkers or imaging techniques to further refine preventive strategies.

In conclusion, early and preventive monitoring of renal function, guided by both traditional measures and urinary biomarkers, constitutes an essential component of comprehensive care in advanced breast cancer patients. Implementing these strategies can effectively reduce the incidence and severity of nephrotoxic complications, ensure continuity of systemic therapy, and enhance overall patient outcomes. These findings provide a solid foundation for the development of standardized preventive diagnostic protocols in oncology practice, ultimately contributing to safer and more effective management of patients undergoing intensive systemic therapy.

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