The Research of Medical Science Review
ISSN: 3007-1208 & 3007-1216 Volume 3, Issue 2, 2025

FREQUENCY OF ACUTE KIDNEY INJURY (AKI) IN PATIENTS PRESENTING WITH NEUTROPENIC COLITIS

Anum Waseem[*1], Summaya Din Bashir[2] Aun Raza[3]

[*1,2]*PG Trainee Internal Medicine, Shaukat Khanum Memorial Cancer Hospital and Research Centre, Lahore*
[3]*Consultant In Infectious Diseases and General/Hospital Medicine, Shaukat Khanum Memorial Cancer Hospital and Research Centre, Lahore*

[*1]dwaseem698@gmail.com

DOI: https://doi.org/10.5281/zenodo.19081307

Keywords
Neutropenic Colitis, Acute Kidney Injury, serum creatinine, urine output, hospital admission

Article History
Received: 06 October 2024
Accepted: 19 December 2024
Published: 05 February 2025

Corresponding Author: *
Anum Waseem

Abstract

Objective: *"To determine the frequency of acute kidney injury in patients admitted with neutropenic colitis"*

Study Design: *Prospective observational study*

Setting and Duration: *Department of Internal medicine at Shaukat Khanum Memorial Cancer Hospital and Research Center, Lahore from 01 April 2024 to 30 September 2024.*

Methodology:

After meeting selection criteria total 73 patients were enrolled and serum creatinine was measured at the time of admission and subsequently at 24-hour intervals for 7 days or until discharge. Urine output was monitored regularly according to hospital guidelines. All patients received management as per the hospital's neutropenic colitis treatment protocol. Acute kidney injury (AKI) was recorded according to the operational definition. Data analysis was performed using SPSS version 21.

Results:

In this research, the mean age of the cases was 50.76 ± 7.05 years, 39 (53.4%) were males and 34 (46.6%) were females. The mean BMI of patients was 21.65 ± 2.66 kg/m². In this study, AKI was observed in 5 (6.85%) patients admitted with neutropenic colitis.

Conclusion: *This research concludes that frequency of AKI among patients admitted with neutropenic colitis was 6.85%*

INTRODUCTION

Cancer is a leading cause of death and a key barrier to increasing life expectancy in every country on the planet[1]. Due to changes in the distribution and frequency of the main risk factors for cancer, some of which are connected to socioeconomic development, as well as population aging and growth, the burden of cancer incidence and death is rapidly rising globally[2]. World Health Organization (WHO) reports that during 2020, Pakistan saw 178388 new cancer diagnoses[3]. Chemotherapy being the mainstay of both curative and palliative treatment of cancer have myriad of side effects. Typical adverse effects include neutropenia due to bone marrow suppression, fatigue, hair loss, peripheral neuropathy, pulmonary and cardiotoxicity [4]. These side effects result in significant number of hospitalizations, complicate treatment and increases morbidity.

Other names for neutropenic colitis include necrotizing enterocolitis, ileocecal syndrome, cecitis, and typhlitis[5]. A clinical condition known as neutropenic colitis was first identified in children with leukemia. Adults suffering from immunosuppressive diseases such AIDS, solid tumor therapy, and hematologic

malignancies like leukemia, lymphoma, multiple myeloma, aplastic anemia, and myelodysplastic syndromes, and organ transplantation, have also been documented to experience it. It is uncertain how often neutropenic colitis really is. According to a 2005 comprehensive analysis, the combined incidence of hospitalized individuals with aplastic anemia, chemotherapy for solid tumors, and hematological malignancies was 5.6%[6]. The reported mortality also ranges with rates as high as 50%[7].

Prevalence of AKI in cancer cases varies. According to a Danish study, incidence of AKI in cancer patients was 17.5%. In particular, it is estimated that incidence of AKI in neutropenic colitis ranges from 1 - 5%. Malignant obstructive uropathy, renal lesions in multiple myelomas, the renal toxicity of antineoplastic medications, and oncologic crises including tumor lysis syndrome, contribute to the renal injury in cancer patients [9, 10]. In Neutropenic colitis, antibiotic therapy, hypovolemia, hypotension and bacteremia are major causes of renal insults. Pathogenesis of AKI is classified in to pre renal, renal (intrinsic) and post renal causes. AKI has significant impact on colitis treatment, prolongs hospital stay, increases requirement of renal replacement therapy and progression to chronic kidney failure.

To date according to our knowledge and understanding we don't have convincing literature or previous study about incidence of AKI in Neutropenic colitis patients in Pakistani population. The coexistence of neutropenic colitis and AKI further worsens prognosis and increases the likelihood of poor outcomes. Monitoring renal function in this group of patients is therefore essential to ensure early detection and timely intervention. Outcomes of this research will help in better understanding of AKI burden and then further studies can be done to identify risk factors, early recognition and treatment of AKI. Determining the prevalence of AKI in cases hospitalized with neutropenic colitis was the aim of this investigation.

METHODOLOGY

The Shaukat Khanum Memorial Cancer Hospital and Research Center's department of internal medicine conducted this prospective observational study, Lahore for a period of 6 months from 01 April 2024 to 30 September 2024, after taking approval from ethical review committee of the hospital (ERC letter number with date). The calculated sample size for this study was 73 taking relevant statistics from previous study stating five percent,[8] prevalence of AKI in Neutropenic colitis patients with 95 % Confidence interval (CI) at 5% margin of error. All the patients were enrolled in this research by applying non-probability consecutive sampling technique.

Inclusion criteria: cases having age range between 18-60 years admitted patients with neutropenic colitis were fall in inclusion criteria. Neutropenic colitis was defined as a clinical condition characterized by the triad of fever, abdominal pain, and neutropenia, with radiological investigations such as ultrasound and CT scan providing additional diagnostic support.

Exclusion criteria: The cases with known chronic kidney disease and BMI greater than 35 kg/m2 were fall in exclusion criteria. After screening for exclusion criteria, patients admitted with diagnosis of and under treatment pathway of Neutropenic colitis were recruited in study.

A base line serum creatinine was measured at the time of admission and then every 24 hour interval for 7 days or till discharge time. Regular urine output charting was done as per hospital guidelines. Urine output of ≤0.5 ml/kg/h for 6 hours, an increase to ≥1.5 times the baseline value (known or assumed to have happened during the preceding 7 days), or a rise in serum creatinine of ≥0.3 mg/dl within 48 hours were all considered indicators of acute kidney injury (AKI). All patients received treatment as per hospital's Neutropenic colitis guideline and pathway.

Analysis was computer based. SPSS version 21 was used. Frequency and percentage were used to determine the prevalence of AKI. For continuous variables like age and serum creatinine, the mean and standard deviation

were computed. Data was stratified for age, gender and BMI of patients and chi-square test was applied to check the association of these effect modifiers on occurrence of AKI. P-value≤0.05 was kept as significant.

RESULTS:

Total of 73 cases were enrolled in this research with a mean age of 50.76 ± 7.05 years. Of these, 39 (53.4%) were males and 34 (46.6%) were females, yielding a male-to-female ratio of 1.14:1. Mean weight was 77.60 ± 7.77 kg, while the mean BMI was 21.65 ± 2.66 kg/m². Regarding serum creatinine, the baseline mean value was 0.56 ± 0.11, which increased to 0.69 ± 0.38 by the 7th day. **Table-I**

In this study, AKI was observed in 5 (6.85%) patients admitted with neutropenic colitis.

Figure-1

Among patients aged ≤45 years, no cases of AKI (AKI) were observed, whereas in those aged >45 years, AKI was noted in 5 (9.1%) patients; however, this difference was not statistically important (p = 0.324). In male patients, AKI occurred in 3 (7.7%) cases compared to 2 (5.9%) cases in females (p > 0.999). Similarly, AKI was found in 5 (7.9%) patients with a BMI ≤25 kg/m², while no cases were observed in cases with a BMI >25 kg/m², a difference that was also statistically insignificant (p > 0.999). **Table-II**

Table-I: Descriptive statistics of demographic and clinical parameters of the cases (n=73)

		Frequency	Percent
Gender	Male	39	53.4
	Female	34	46.6
Age (Years)		50.76±7.05	
Weight (Kg)		77.60±7.77	
BMI (Kg/m^2)		21.65±2.66	
Sr. Creatinine at baseline		0.56±0.11	
Sr. Creatinine after 7th day		0.69±0.38	

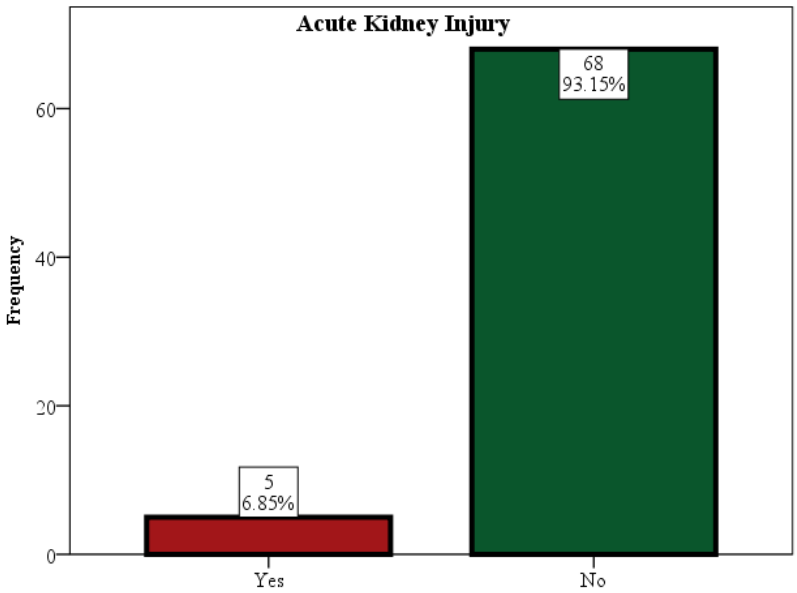

Figure-1: Frequency of AKI among cases admitted with neutropenic colitis (n=73)

Table-II: Comparison of AKI in cases Admitted with Neutropenic colitis between age, gender, weight and BMI status of the patients

		AKI		p-value
		Yes	No	
Age	≤ 45 years	0 (0%)	18 (100%)	0.324
	>45 years	5 (9.1%)	50 (90.9%)	
Gender	Male	3 (7.7%)	36 (92.3%)	>0.999
	Female	2 (5.9%)	32 (94.1%)	
BMI	≤25 Kg/m2	5 (7.9%)	58 (92.1%)	>0.999
	>25 Kg/m2	0 (0%)	10 (100%)	

DISCUSSION:

In this study, AKI was observed in 5 (6.85%) patients admitted with neutropenic colitis. Some of the studies are discussed below showing their results as. Due to the variable age groups included in various studies and the diverse presentation of neutropenic enterocolitis, the actual incidence of the condition varies greatly, ranging from 0.8% to 26%[11, 12]. In past studies, neutropenic enterocolitis was characterized as a concerning complication in the oncologic case group, with death rates varying between 50% and 100%[13].

When neutropenia is present, the uncommon and potentially fatal illness known as neutropenic enterocolitis is marked by fever and stomach discomfort. Oncologic patients who are severely neutropenic due to cytotoxic treatment are more likely to experience it. Seldom has neutropenic enterocolitis been documented in the literature as a side effect of rheumatoid arthritis (RA) medication. We report on a RA patient who experienced neutropenic enterocolitis as a side effect of taking methotrexate[14].

Pediatric hematooncology patients sometimes have adverse drug reactions, such as febrile neutropenia. It is unusual for pediatric patients who are feverish and neutropenic to develop AKI after receiving high doses of methotrexate and combination antibiotic treatment with piperacillin-tazobactam + vancomycin. Acute renal damage brought on by the combination of vancomycin and piperacillin is described in literature[15-17].

A pooled incidence of 5.6% was found in a 2005 comprehensive study of patients with aplastic anemia, cases receiving treatment for solid tumors and hospitalized adults with hematological malignancies. Mortality rates that were reported ranged from 50% to 50%[7]. According to Hatice Duygu Bas et al., when vancomycin and piperacillin were used together, the incidence of AKI was higher than when they were used alone[18]. In contrast to monotherapy with vancomycin or meropenem, another research by Kevin O'Callaghan et al. that used a retrospective cohort of ICU patients similarly found a higher prevalence of vancomycin and piperacillin-induced AKI[15]. The same results were found in another prospective cohort of ICU patients by Todd A. Miano et al. that connected the rise in serum creatinine following cure with piperacillin and tazobactam, vancomycin[17].

One study Natacha Kapandji by et al[19] determined that among onco-hematological patients who frequently need intensive care unit hospitalization, neutropenic entero-colitis is a common and underreported consequence of neutropenia. The pathophysiology of NE has to be reexamined in light of recent discoveries on gut microbiota and its role in maintaining the integrity of the intestinal barrier and inflammatory response. Improved knowledge of the processes behind neutropenic enterocolitis might lead to better patient care[19].

The significance of marginated versus interstitial neutrophils in pathophysiology of AKI is emphasized by Awad et al. Since measures to lower this population of neutrophils enhance renal function in AKI, findings have highlighted the critical role of the transmigrated neutrophil, which has distinct phenotypic traits and is not only an innocent or "neutral" bystander[20]. Only one incidence of neutropenic enterocolitis, an uncommon side effect of RA medication, has been documented in English-language literature. The first instance of neutropenic enterocolitis in a 69-year-old RA

patient after sulphasalazine treatment was reported by Chakravarty et al[21].

The most significant risk factor for myelosuppression seems to be renal failure. MTX is mostly removed by the kidney's proximal tubular secretion and glomerular filtration. Reduced MTX excretion and consequent serum buildup in the presence of renal impairment may result in bone marrow suppression or other toxicities. It has been proposed that if the anticipated creatinine clearance rate is less than 30 milliliters per minute, low-dose MTX should not be administered, although there is no data to support dosage adjustments for patients with renal impairment[22].

CONCLUSON:

On the basis of this study we may conclude that frequency of AKI was 6.85% in patients admitted with neutropenic colitis.

REFERENCES:

1. Bray F, Laversanne M, Weiderpass E, Soerjomataram I. The ever-increasing importance of cancer as a leading cause of premature death worldwide. Cancer 2021;127(16):3029-30. https://doi.org/10.1002/cncr.33587.
2. Omram AR. The epidemiologic transition: a theory of the epidemiology of population change. Bulletin of the World Health Organization 2001;79(2):161-70.
3. gco.iarc. Data visualization tools for exploring the global cancer burden in 2022 2022 [cited 2025]. Available from: vhttps://gco.iarc.fr/today/en.
4. Pearce A, Haas M, Viney R, Pearson S-A, Haywood P, Brown C, et al. Incidence and severity of self-reported chemotherapy side effects in routine care: A prospective cohort study. PloS one 2017;12(10):e0184360. https://doi.org/10.1371/journal.pone.
5. Nesher L, Rolston KV. Neutropenic enterocolitis, a growing concern in the era of widespread use of aggressive chemotherapy. Clinical infectious diseases 2013;56(5):711-7. https://doi.org/10.1093/cid/cis998.
6. Gorschlüter M, Mey U, Strehl J, Ziske C, Schepke M, Schmidt-Wolf IG, et al. Neutropenic enterocolitis in adults: systematic analysis of evidence quality. European journal of haematology 2005;75(1):1-13. https://doi.org/0.1111/j.600-0609.2005.00442.x.
7. Ullery BW, Pieracci FM, Rodney JR, Barie PS. Neutropenic enterocolitis. Surgical infections 2009;10(3):307-14. https://doi.org/10.1089/sur.2008.061.
8. Sazanami K, Inose R, Dote S, Horiuchi N, Kobayashi Y, Muraki Y. Combination therapy of vancomycin and piperacillin/tazobactam in adult febrile neutropenia patients with haematopoietic malignancies increases the risk of acute kidney injury regardless of vancomycin trough concentration. Journal of Chemotherapy 2021;33(6):440-2. https://doi.org/10.1080/1120009X.2020.848298.
9. Libório AB, Abreu KLS, Silva J, Geraldo B, Lima RS, Barreto AG, Barbosa OA, et al. Predicting hospital mortality in critically ill cancer patients according to acute kidney injury severity. Oncology 2011;80(3-4):160-6. https://doi.org/10.1159/000329042.
10. Christiansen CF, Johansen MB, Langeberg WJ, Fryzek JP, Sørensen HT. Incidence of acute kidney injury in cancer patients: a Danish population-based cohort study. European journal of internal medicine 2011;22(4):399-406. https://doi.org/10.1016/j.ejim.2011.05.005.
11. Miller EE, Reardon LC. Neutropenic Enterocolitis in a Pediatric Heart Transplant Recipient on Multiple Immunosuppressants. Case Rep Transplant 2018;2018:3264921. DOI: 10.1155/2018/.
12. Sachak T, Arnold MA, Naini BV, Graham RP, Shah SS, Cruise M, et al. Neutropenic Enterocolitis: New Insights Into a Deadly Entity. Am J Surg Pathol 2015;39(12):1635-42. DOI: 10.097/PAS.0000000000000517.

13. Alt B, Glass NR, Sollinger H. Neutropenic enterocolitis in adults. Review of the literature and assessment of surgical intervention. Am J Surg 1985;149(3):405-8. DOI: 10.1016/s0002-9610(85)80119-7.
14. Lin Y, Chen H, Chen P. Neutropenic enterocolitis associated with methotrexate therapy for rheumatoid arthritis: a case report. J Arthritis 2014;3(02):126.
15. O'Callaghan K, Hay K, Lavana J, McNamara JF. Acute kidney injury with combination vancomycin and piperacillin-tazobactam therapy in the ICU: a retrospective cohort study. International Journal of Antimicrobial Agents 2020;56(1):106010. https://doi.org/10.1016/j.ijantimicag.2020.
16. Blair M, Côté J-M, Cotter A, Lynch B, Redahan L, Murray PT. Nephrotoxicity from vancomycin combined with piperacillin-tazobactam: a comprehensive review. American journal of nephrology 2021;52(2):85-97. https://doi.org/10.1159/000513742.
17. Miano TA, Hennessy S, Yang W, Dunn TG, Weisman AR, Oniyide O, et al. Association of vancomycin plus piperacillin–tazobactam with early changes in creatinine versus cystatin C in critically ill adults: a prospective cohort study. Intensive Care Medicine 2022;48(9):1144-55. DOI: 10.007/s00134-022-6811-0.
18. Bas HD, Baser K, Yang S. Acute kidney injury associated with concomitant use of vancomycin with piperacillin-tazobactam: a focused review and meta-analysis. The Southwest Respiratory and Critical Care Chronicles 2016;4(15):32-7. doi:10.12746/swrccc2016.0415.198.
19. Kapandji N, Azoulay E, Zafrani L. Recent advances in neutropenic enterocolitis: Insights into the role of gut microbiota. Blood reviews 2022;54:100944.
20. Awad AS, Rouse M, Huang L, Vergis AL, Reutershan J, Cathro HP, et al. Compartmentalization of neutrophils in the kidney and lung following acute ischemic kidney injury. Kidney international 2009;75(7):689-98. https://doi.org/10.1038/ki.2008.648.
21. Chakravarty K, Scott D, McCann B. Fatal neutropenic enterocolitis associated with sulphasalazine therapy for rheumatoid arthritis. Rheumatology 1992;31(5):351-3.
22. Saag KG, Teng GG, Patkar NM, Anuntiyo J, Finney C, Curtis JR, et al. American College of Rheumatology 2008 recommendations for the use of nonbiologic and biologic disease-modifying antirheumatic drugs in rheumatoid arthritis. Arthritis Care & Research: Official Journal of the American College of Rheumatology 2008;59(6):762-84. https://doi.org/10.1002/art.23721.