Prevalence of urinary tract infections and sterile pyuria among Chronic Kidney Disease Patients.

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ABSTRACT:

Objective: To determine the prevalence of urinary tract infections and sterile pyuria among patients in the nephrology department with chronic kidney disease.

Methodology: It is a prospective observational study carried out in six months at Dow University Hospital in Karachi and involving 263 patients with chronic kidney disease (CKD) with ages between 18 and 92 years. To analyze the data, we used SPSS Statistics version 25 offered by IBM. To identify any risk factors, the research team analyzed the information using descriptive statistics, the Chi-square test, stratified analysis, and logistic regression.

Results: Pyuria was present in 30.4 % of those tested, and 12.9 % were found to have UTIs, but 17.5 % were positive for sterile pyuria. It was observed that CKD stage had a strong relationship with sterile pyuria (p = 0.010), but not UTIs (p = 0.436). No statistically significant differences were identified when the group was compared according to age (adults vs. children). The age seems to be slightly related to sterile pyuria with a p-value of 0.056. Among such culture-positive cases, the greatest number was attributed to bacteria known as Escherichia coli, which infected 50.0 % of the patients.

Conclusion: Sterile pyuria is very common among patients with CKD and is strongly associated with the severity of the disease. The occurrence of antimicrobial resistance in bacteria affecting the urinary tract Infections is of great concern. The findings imply that future research on larger populations should be conducted to investigate the implications of these findings on patient care and outcomes.

Keywords: Chronic kidney disease, Escherichia coli, Urinary tract infection, Sterile pyuria.

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Introduction:

Chronic kidney disease (CKD) is prevalent in primary care, and it is characterized by a gradual loss of kidney functions that occur over months or years.[1] With diabetes and hypertension becoming increasingly prevalent in the global population, more individuals are suffering CKD[2], and because of this illness, death and disability are expected to rise globally by 2040.[3] In Pakistan, around 23.3 % of adults are affected by CKD, and its prevalence differs according to age, gender, and the ways of defining it.[4] As diabetic kidney disease is a frequent cause of end-stage kidney disease, it is essential to classify it correctly to find the most effective treatment and prognosis.[5, 6] CKD can be asymptomatic at first and then develop fatigue, anorexia, oedema, and vomiting; the impaired immune system and the malfunction of the renal organ can predispose a patient to severe UTIs. Studies have established that older patients with kidney disease are more prone to UTIs, and in older individuals, as well as youth, kidney stones cause upper UTIs.[7, 8] CKD individuals who are mainly on dialysis or have undergone graft surgery may experience UTIs more than others, and they require special approaches to care, as their immune defenses are compromised and new strain of bacteria are emerging as more prevalent.[9] It is not always possible to limit infection within the bladder; it can also reach the kidneys, and it is important to diagnose using physical examination and a urine test and provide standard anti-infection drugs. UTIs are frequent in CKD patients, as well as in older patients. In the 129 CKD cases, it was found that patients aged more than 60 years had the highest incidence of UTIs. Escherichia coli was also the most frequent in all age and gender groups, then by Klebsiella and Pseudomonas. In the majority of instances, the infection was caused by a single type of microorganism; gram-negative bacteria were the most frequent. The most frequently reported problems in patients included pain during urination and the feeling of the necessity to urinate too frequently.[10]

UTI is frequent among individuals with CKD, as the literature indicates that their risk ranges between 13.4%. And 15.8%.[11, 12] Approximately 60 % of patients are forced to cope with recurrent infections.[13] Typically, during urination, a burning sensation and a strong desire to urinate are observed in 63 % of individuals, and occasional fever (23%), stomach pain (11%), and some unexplained symptoms in 3 %. Otherwise, the female infections may lead to severe conditions like sepsis. Quinolones and cotrimoxazole are continued to be used; however, unfortunately, the action of this is also reduced in individuals with unhealthy kidney functions, and since gram-negative bacteria are even more resistant to drugs, that leads to the emergence of another issue in treatment.[12, 14] Despite the increased understanding of medical sciences, limited reports on urinary tract in-

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fection and sterile pyuria in hospitals where people with chronic kidney disease are treated in Pakistan are available. Through this information, doctors will be able to make good decisions for their patients, treat them with antibiotics. The aim of the research was to identify UTIs and sterile pyuria among CKD patients and to identify the factors that affect them.

Objectives:

To determine the prevalence of urinary tract infections among and sterile pyuria among patients of chronic kidney disease patients. At the same time we will identify antimicrobial resistant pattern of urinary pathogens and impact of UTI/sterile pyuria on the progress of CKD and morbidity.

Methodology:

This study was conducted in the Department of Medicine and Nephrology of Dow University Hospital, Ojha Campus, following the consent of the institutional review board (IRB) of the Dow University of Health Sciences, Karachi (Ref: IRB-3772/DUHS/approval/2024/07). The research was done during January 2025 to June 2025. During period of study patients were selected using non-probability consecutive convenience sampling and 263 patients, aged 18-92 years, of CKD were recruited. These patients were selected from inpatient and outpatients units. The diagnosis of CKD was based in accordance with the KDIGO 2024 criteria[15], whereas the concepts of pyuria, UTI, and sterile pyuria were defined in accordance with the standard diagnostic criteria.[16, 17] To ensure the validity of the study, the subjects with other disease conditions or those who have undergone surgery in the recent past that could have had an impact on their urinary outcome were excluded. Each participant was given informed consent in written form prior to being included in the study.

The sample size of 263 participants was calculated with the use of the Open Epi online sample size calculator (version 3.01) using a calculated prevalence (p) of 21.8% of pyuric CKD patients in a prior study involving a similar population,[11] at a 95 % confidence level, and a margin of error of 5. The privacy of the participants was guaranteed, and the procedures of the study were completely described to the participants. Each subject was assessed according to a standardized protocol, and the results were noted on a specially developed form for this research.

All the enrolled patients had their urine samples collected aseptically to undergo routine microscopy, dipstick analysis, and urine culture. A positive leukocyte esterase test and 10 or more white blood cells/mm3 in non-centrifuged urine or 3 or more white blood cells/high power field in centrifuged urine were as pyuria. When a urine culture revealed 100,000 CFU/mL of one of the pathogenic organisms, it was classified as a urinary tract infection (UTI). Pyuria was found to be sterile in cases of the presence of pyuria with little or no bacteria. The rest of the data recorded in the course of the study included the age of the subject, gender, CKD stage (calculated based on estimated glomerular filtration rate), symptoms (dysuria, urinary frequency, and fever), comorbidities, and a history of UTIs in the past. The follow-up done at outpatient clinic or in case patient readmitted in the hospital. All data was entered digitally and periodically reviewed to determine the accuracy and completeness of the data.

Analysis of the data was done using IBM SPSS Statistics version 25. Descriptive statistics were used to summarize the findings. Means, medians, and standard deviations were provided in continuous variables, whereas the categorical variables were gender, educational status, CKD stage, UTI status, sterile pyuria presence, and resistance to specific antimicrobials. The chi-square test has been employed to find out whether there was a relationship between CKD stage and either UTI or sterile pyuria. Binary logistic regression was performed to identify relevant variables with the aim of identifying independent risk factors in reference to UTI as well as sterile pyuria. The percentages of antibiotic resistance in patients were also established by analysis. The effect modifiers were age, gender, and CKD stage, which were controlled through the use of stratification and post-stratification chi-square test to determine the statistical significance. All the analyses turned out to be statistically significant at a p-value of less than 0.05.

Results:

The sample size was 263 adults with chronic kidney disease (CKD). Among these patients, 41.83 % were in stage G4, 29.28 % in stage G5, 21.3 % in stage G3b, 5.7 % in stage G3a, 1.52 % in stage G2, while 0.38 % in stage G1. The mean age of participants of the study was 60.11 ± 14.87 years (median 62 years; 14.87 standard deviation) of age. The male were 55.13%, female were 44.87% among study population. Regarding educational attainment, 40.3% had a degree, 33.46% had a secondary education, 16.73% had a primary education, 7.22% had no education, and 2.28% had a postgraduate degree. 60% of the patients had hypertension, with 51.4 % having diabetes. One out of every three participants had pyuria, 13 % had UTIs, and 17 % had sterile pyuria. The average eGFR of this group was 23.75 mL/min/1.73 m^2 (median 21 mL/min/1.73 m^2; SD 13.42 mL/min/1.73 m^2). The mean years of CKD were 5.38 + 3.27 years (Table 1).

Table 1: Demographic and Clinical Characteristics of the Study Population.

Variable	Percentage/Mean ± SD
Male	55.13%
Female	44.87%
Mean Age	60.11 ± 14.87 years
Hypertension	60.8%
Diabetes Mellitus	51.4%
Mean eGFR	23.75 ± 13.42 mL/min/1.73 m² M
Mean CKD Duration	5.38 ± 3.27 years

Among 263 CKD patients, 80 (30.4%) had pyuria. There was no significant difference in the distribution of men and women in those with and without pyuria. A large discrepancy was observed in age, though; patients with pyuria were older (mean age of 63.38 ± 15.36), compared to those without pyuria (mean age of 58.69 ± 14.46). There was also a significant difference in the means of eGFR, whereby the mean of the eGFR in patients who were pyuric (26.64 mL/min/1.73 m^2) was higher than the mean of the eGFR in the non-pyuric patients (22.49 mL/min/1.73 m^2), with a p-value of less than 0.05.

Patients who had pyuria were better placed in CKD stage G4 and G3b, and patients with no pyuria were placed in G5 (Table 2). An Important relationship between pyuria and the stage of CKD was detected. Out of 80 pyuric CKD patients, 34 of them had confirmed UTIs, and 46 did not indicate infection. The results show that age and gender did not have a significant effect on the rate of pyuria or UTI. UTI patients with pyuria were more likely to be at advanced stages of CKD. Even though the mean eGFR in sterile pyuria (27.48 mL/min/1.73 m^2) was slightly greater than that in

UTI-related pyuria (25.50 mL/min/1.73 m^2), the difference did not reach the level of statistical significance (Table 3).

Table No 2: Comparison Between Pyuric and Non-Pyuric CKD Patients

Variable	Pyuric Group	Non-Pyuric Group
Mean Age	63.38 ± 15.36	58.69 ± 14.46
Male	52.5%	56.28%;
Female	47.5%	43.72%
Mean eGFR	26.64±13.53	22.49 ±13.20
Most Common CKD Stage	G4 (42.5%)	G5 (33.33%)

Table No 3: Comparison Between UTI and Sterile Pyuria in CKD Patients

Variable	UTI-Associated Pyuria	Sterile Pyuria
Mean Age	61.91 ± 16.05	64.46 ± 14.92
Female (%)	38.24%	54.35%
CKD Stage G4	52.94%	34.78%
CKD Stage G5	17.65%	21.74%
Mean eGFR	25.50 ± 11.75	27.48 ± 14.77

Discussion:

The present study may help us in identifying the prevalence of pyuria, sterile pyuria, and UTIs among individuals with CKD, risk factors involved, and the antimicrobial resistance patterns exhibited by these individuals. Pyuria was observed most frequently among the patients (30.41%), and more frequently had sterile pyuria (17.49%), as compared to patients with UTIs (12.93%). Thus, it may be observed that CKD patients who are positive for pyuria may not experience the typical UTI, which occurred in 35 % of CKD cases in another study.[18] Findings are consistent with a published study reporting that sterile pyuria is common in CKD and could be due to inflammation in the kidney, interstitial nephritis, or other diseases. Additionally, it has previously been found that sterile inflammation can be observed earlier in the course of CKD, prior to many nephrons being lost.[19] It emerged that CKD patients were at risk of sterile pyuria, indicated by chi-Square test for the relationship between these two entities x^2 (4) = 3.7845 (p=0.0105). In the case of age and gender, the correlation between the variables was not significant, which could imply that the variables were not accurately measured and may have been influenced by some confounding variables. They found that the age of the pyuric patients was larger (mean of 63.38 years vs. 58.69 years in non-pyuric patients, p = 0.0218), and a slightly larger mean eGFR (26.64 mL/min/1.73 m² vs. 22.49 mL/min/1.73 m² in non-pyuric patients, p = 0.0226). This observation indicates that pyuria does not necessarily arise as a result of deteriorating renal performance and implies that additional investigations are required to understand whether inflammation, immune modulations, or tubular mischief in CKD have any role to play. In their study, Almaiman et al. also found that pyuria and sterile pyuria are rather common in late-stage CKD patients, which demonstrates that this issue can be a predictor of a more severe health condition.

Although this study found a correlation between sterile pyuria and stages of CKD, no definitive correlation was found between CKD and UTI, nor between any individual risk factor of UTI and CKD. However, UTI patients were in molate-stage CKD (G4) and had with lower average eGFR, but the results were not statistically significant. It means that sterile pyuria occurrence is more frequent, but UTIs could also be a significant issue in advanced CKD because of such factors as abnormal urination, weak immunity, and frequent interactions with medical personnel. Similar to the results of the earlier studies, we also find that higher numbers of CKD patients had sterile pyuria than UTIs (17.49% vs. 12.93%), which is comparable to 30.5% of asymptomatic pyuria in CKD as reported by Kwon et al, with only 70% of them being bacteria-positive. Their evidence also confirms that sterile pyuria is more likely to rise with worsening CKD, as was also the case with our data, since more sterile pyuria was observed in later stages, but these differences were not statistically significant following the stratification. Kwon et al. indicate that most white blood cells detected in sterile pyuria are typically neutrophils, and this percentage is a bit higher than that observed with UTI cases; thus, slow inflammation, and not infection, may be the reason that makes urine look cloudy in CKD.[20] We must not therefore always treat the pyuria in CKD with antibiotics, as that only increases the antibiotic resistance in the patient, and would not benefit the patient.[21]

Pyuric patients were significantly older than those without elevated leukocytes in urine (mean age: 63.38 vs. 58.69 years, p = 0.0218), as it is reported by other studies as well.[22] It was observed that the mean eGFR of the pyuric group was more than the mean of the other group (26.64 mL/min/1.73 m² vs. 22.49 mL/min/1.73 m 2, p = 0.0226). This research contradicts the common belief that the term pyuria is associated with increased kidney problems and recommends that leukocyturia be handled cautiously in patients without bacterial infections.

Escherichia coli (50.00%), Enterococcus spp. (32.14%), and Klebsiella pneumoniae (14.29) were the three most common uropathogens in this study, as they are in most of the world.[23] Nevertheless, with regard to the trends in drug resistance, some of them included: E. coli bacteria can resist the influence of ampicillin, ciprofloxacin, and cotrimoxazole. Some bacterial isolates have Enterococci that are resistant to vancomycin. These resistant Enterococcus bacteria are an issue because not many drugs are provided to patients with drug-resistant organisms in CKD, and there is no easy way to modify the dosing to consider the kidney functionality.[21] It has been identified that Klebsiella pneumoniae is resistant to amoxicillin/clavulanic acid and certain cephalosporins. The findings indicate that urine culture-guided treatment is highly significant among CKD patients, as treating them without the latter may not be effective and may even intensify resistance.[9, 14] Moreover, the dose of medications should be adjusted as nitrofurantoin and Cotrimoxazole are not necessarily effective in treating advanced CKD (those with eGFR below 50 mL/min).[21]

Of concern was the trend of antimicrobial resistance. Similar to the recent surveillance reports, E. coli and Klebsiella demonstrated that they are resistant to the most frequently used antibiotic agents of ampicillin and fluoroquinolones.[24, 25]

The fact that numerous cases (17.49%) show urine free of bacteria but with white blood cells present is clinically significant. This may be due to chronic inflammation of the kidney, often a result of CKD. The availability of antibiotics can be misleading and give a false impression. Renal tu-

berculosis and viral cystitis are examples of non-bacterial infections. Issues with the sample or sampling method can also cause this. Since CKD is linked to inflammation, sterile pyuria might result from kidney changes rather than an actual infection.[26] In CKD, persistent inflammation can increase white blood cells in urine without infection. However, without a renal biopsy, imaging, or TB-PCR, the true causes of sterile pyuria are only speculative. Therefore, clinicians should prescribe antibiotics only when necessary and consider additional tests like PCR and imaging in persistent cases.[20]

However, there are certain weaknesses to this study. Due to the cross-sectional nature, we cannot conclude that sterile pyuria leads to the aggravation of CKD. The study did not involve a large number of patients, which could have failed to establish weaker links, particularly between various groups of patients. The results may not be generalized to all or the majority of CKD patients due to the fact that this study was done in one Centre. Although the study excludes patients after recent catheterization, uncontrolled diabetes, or treatment that leaves the immune system weakened, which would improve the findings' control, this approach will constrain the study's utility in a practical clinical setting, as these latter conditions are not uncommon among actual patients. More research, inclusive of numerous centers and longitudinal studies, must be conducted to understand more about the cause of sterile pyuria in CKD and the potential to predict or control the disease.

Conclusion

To investigate sterile pyuria and how it affects the clinical outcome, researchers should conduct long-term studies of CKD patients. By using PCR and next-generation sequencing, we may be able to identify infections that have never been observed before or learn about immune responses that cause leukocyturia. In a similar vein, research that aims to prevent other causes of pyuria and choose the best medicines more regularly can help these individuals and prevent the needless prescription of antibiotics.

Conflict of Interest: None

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Sooraj Kumar	conception and design, acquisition of data, analysis, interpretation of data
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