Research Article

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Chronic urothelial inflammation associated with UTI in women: A Clinicopathological study

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Abstract

Objective:

Chronic urothelial inflammation associated with urinary tract infections (UTIs) in women presents a significant clinical challenge, often leading to recurrent episodes and potential complications. The main objective of this study was to find the clinicopathological correlation of chronic urothelial inflammation associated with UTI in women.

Material and Methods:

This cross-sectional study was conducted in Urology Department, Shifa International Hospital Islamabad from 2022-2023. Data were collected from 220 female patients suffering from UTI. Data were collected from 220 female patients according to inclusion and exclusion criteria. All the demographic and clinical data were noted on systematically designed questionnaire. Medical history, clinical symptoms and imaging findings were also extracted from hospital record.

Results:

Data were collected from 220 female patients. Mean age was 45.6 ± 10.2 years and mean BMI was 26.8 ± 3.5kg/m^2. Hypertension was the most prevalent comorbidity at 35%, followed by diabetes mellitus at 20% and chronic kidney disease at 10%. Recurrent UTIs were reported by 60% of participants, while 40% experienced their first-time UTI. The treatment outcomes were predominantly favorable, with 90% of patients showing a positive response. Symptoms resolved within 7-10 days for most cases, indicating an effective therapeutic intervention. However, 10% of patients required hospitalization, suggesting the severity of their condition or the need for more intensive management strategies.

Conclusion:

Chronic urothelial inflammation is prevalent among women with urinary tract infections (UTIs), characterized by lymphocytic infiltrate and a microbiological profile dominated by Escherichia coli.

Keywords: *UTI, Women, Infection, Inflammation, Therapeutics*

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INTRODUCTION

Chronic urothelial inflammation associated with urinary tract infections (UTIs) in women presents a significant clinical challenge, often leading to recurrent episodes and potential complications. Despite being a common condition, the clinicopathological features and underlying mechanisms of chronic urothelial inflammation in UTI remain poorly understood. Recurrent UTI is a rather uncomfortable and one of the most common concerns in the urogynecology office (Aalam et al., 2022). Recurrent UTI is diagnosed when a woman has at least 3 symptomatic and medically confirmed episodes of the infection in the last 12 months, and this is in conjunction of the IUGA/ICS joint report on the terminology for female pelvic floor dysfunction. The previous UTI(s) should have cleared before a new UTI is diagnosed the previous UTI(s) should have resolved prior to a further UTI being diagnosed. Recurrent UTI is currently among the most often cited conditions associated with female pelvic floor dysfunction. Bladder pain syndrome / interstitial cystitis (IC/BPS) is defined as a chronic inflammatory disease of the urinary bladder that has been reported to affect millions of people. Histology demonstrated that it developed by IC/BPS patients are infiltrated with mast cells,

befitting a disease driven by immune dysfunction (Hasan et al., 2021). Bladder oversensitivity based on a great number of studies is well described through a primary urothelial lining defect in chronic cystitis. Based on our study group, we have provided evidence of urothelial barrier dysfunction, and chronic inflammation and possibly the pathophysiological factor for increased urothelial apoptosis. Overactive Bladder (OAB) is yet again a topic that is to be associated with chronic bladder inflammation (Akiyama et al., 2020). Quoting inflammatory biomarker, including nerve growth factor (NGF), cytokines, and serum C-reactive protein, the phenomenon of OAB as well as IC/BPS has been validated by present studies Recurrent UTI is recognized as a very bothersome and frequently encountered complaint in the urogynecology clinic. As per the IUGA/ICS joint report classification of female pelvic floor dysfunction, recurrent UTI is further characterized as occurrences of three or more symptomatic and previously medically confirmed UTI in a period of 12 months (Htoo et al., 2023). The further UTI is supposed to occur when the previous UTI(s) should have resolved entirely. The prevalence of female pelvic floor dysfunction and its correlation with recurrent UTI in summary, recurrent UTI is one of the main diagnoses of female pelvic floor dysfunction (Martin et al., 2022).

Since OAB has similar manifestations as other frequent urological diseases, including recurrent UTI, the overwhelming number of women with OAB are diagnosed as UTIs and empirically treated with antibiotics, without following a urine culture procedure as standard. Still, if urine cultures are done fewer than half the ladies are likely to have a positive culture implying that the acceptance of empiric treatment to UTIs without necessarily carrying out cultures, often results in a misdiagnosis of UTI (Clark et al., 2023). Nonetheless, accumulating data suggest that such chronic low-grade bacterial bladder colonization may worsen OAB symptoms and could theoretically serve to explain why prior OAB management approaches have not been sufficient. As for patients with OAB that remains uncontrolled by conventional pharmacotherapy encompassing antimuscarinics and beta-3 adrenoceptor agonist, mirabegron, employing molecular methods including 16S RNA sequencing and extra culture approaches, about organisms that might underlie persistent OAB signs may be identified (Vuruşkan et al., 2021). ESRD patients are likely to have reduced bladder capacity and awareness of the fullness of the bladder. It was clear from the data obtained that patients on chronic dialysis generally had LUTS which includes BO or difficulty in urinating as stated by Lagarde et al., (2022). Recurrent UTI may also be accompanied by bladder irritative symptoms among identified patients. Prior studies have shown the PT UTIL is higher among patients with recurrent UTI, and this indicates that there is chronic inflammation in the bladder of such patients once the UTI infection is over (Seitz et al., 2022).

The main objective of this study was to find the clinicopathological correlation of chronic urothelial inflammation associated with UTI in women.

MATERIALS & METHODS

This cross-sectional study was conducted in Urology Department, Shifa International Hospital Islamabad from 2022-2023. Data were collected from 220 female patients suffering from UTI.

Inclusion criteria:

- Female patients with confirmed diagnosis of UTI.
- Confirmed diagnosis of chronic urothelial inflammation.
- Willing to participate in the study

Exclusion criteria:

- Patients with incomplete medical record and UTI with other comorbidities were excluded from the study.

Data collection: Data were collected from 220 female patients according to inclusion and exclusion criteria. All the demographic and clinical data were noted on systematically designed questionnaire. Medical history, clinical symtpms and imaging findings were also extracted from hospital record. The variables including chronic kidney disease (CKD) or end-stage renal disease (ESRD), presence or absence of anuria, history of urinary bladder carcinoma (UCC), occurrence of intermittent urinary tract infections (UTIs), and clinical manifestations of bladder discomfort were also recorded. Each patient received detailed information about the study rationale and procedures, and written informed consent was obtained prior to cystoscopy and bladder biopsy procedures.

Statistical analysis: The collected data were analyzed using SPSS v27. The significant value for $P < .05$ was accepted as statistically significant.

RESULTS

Data were collected from 220 female patients. Mean age was 45.6 ± 10.2 years and mean BMI was 26.8 ± 3.5kg/m^2. Hypertension was the most prevalent comorbidity at 35%, followed by diabetes mellitus at 20% and chronic kidney disease at 10%. Recurrent UTIs were reported by 60% of participants, while 40% experienced their first-time UTI. Clinical symptoms were prominent, with

dysuria being the most prevalent at 80%, followed by frequency at 75%, urgency at 70%, and hematuria at 50%.

Table 1: Demographic data of patients

Demographic/Baseline Parameters	Values (Mean ± SD or Percentage)
Age (years)	45.6 ± 10.2
Body Mass Index (kg/m^2)	26.8 ± 3.5
Comorbidities	
- Hypertension	35%
- Diabetes mellitus	20%
- Chronic kidney disease	10%
UTI History	
- Recurrent UTIs	60%
- First-time UTIs	40%
Clinical Symptom	
Dysuria	80%
Frequency	75%
Urgency	70%
Hematuria	50%

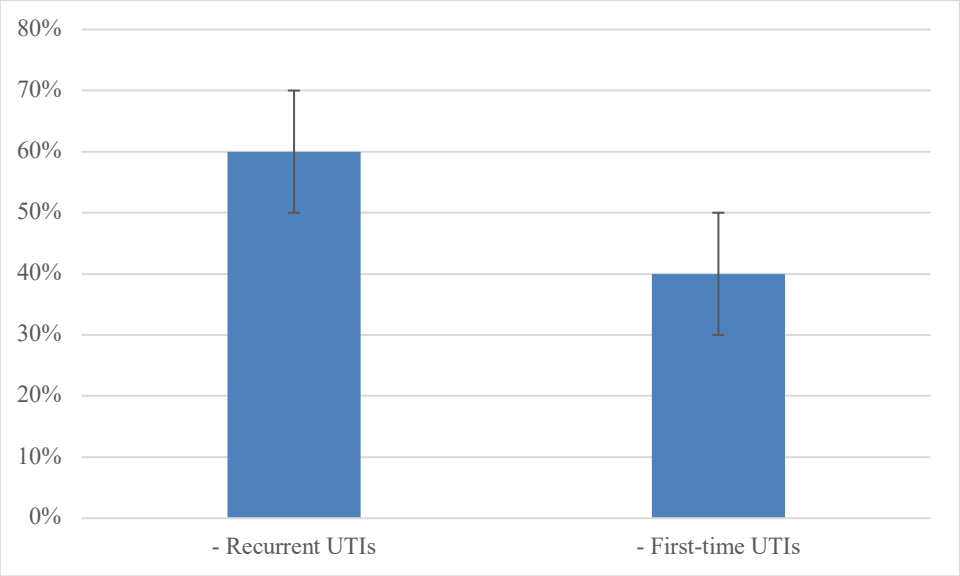


Figure 1. Frequency of the UTI found during history

Predominant inflammatory infiltrate consisting of lymphocytes in 60% of cases, neutrophils in 30%, and macrophages in 10%. Among the identified pathogens, Escherichia coli was the most common, found in 60% of cases, followed by Klebsiella pneumoniae at 20%, Enterococcus faecalis at 10%, and other pathogens collectively accounting for the remaining 10%.

Table 2: Histopathological and microbiological findings

Finding	Prevalence (%)
Chronic Urothelial Inflammation	100%
Predominant Inflammatory Infiltrate	
- Lymphocytes	60%
- Neutrophils	30%
- Macrophages	10%
Pathogen	
Escherichia coli	60%
Klebsiella pneumoniae	20%
Enterococcus faecalis	10%
Others	10%

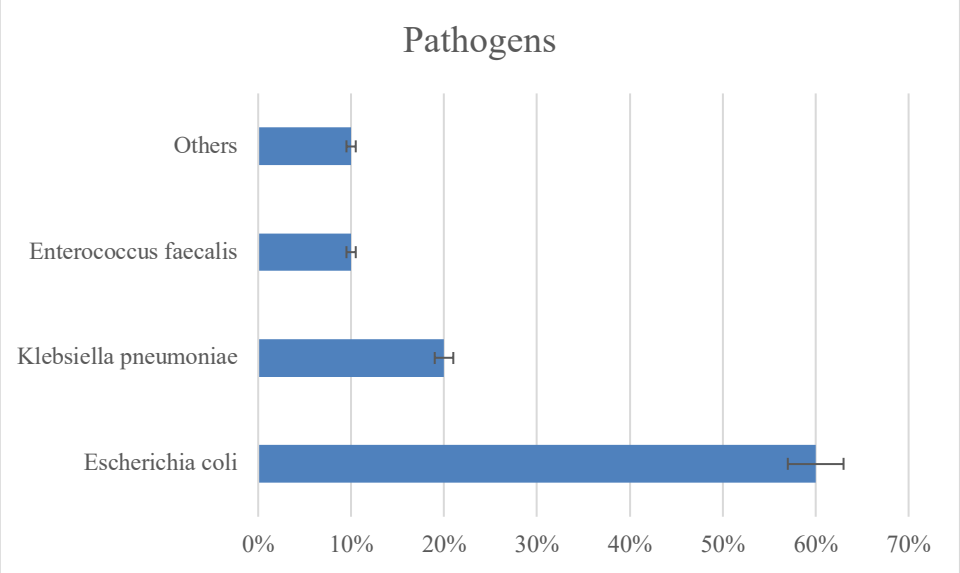


Figure 2. Frequency of the pathogen found in UTI

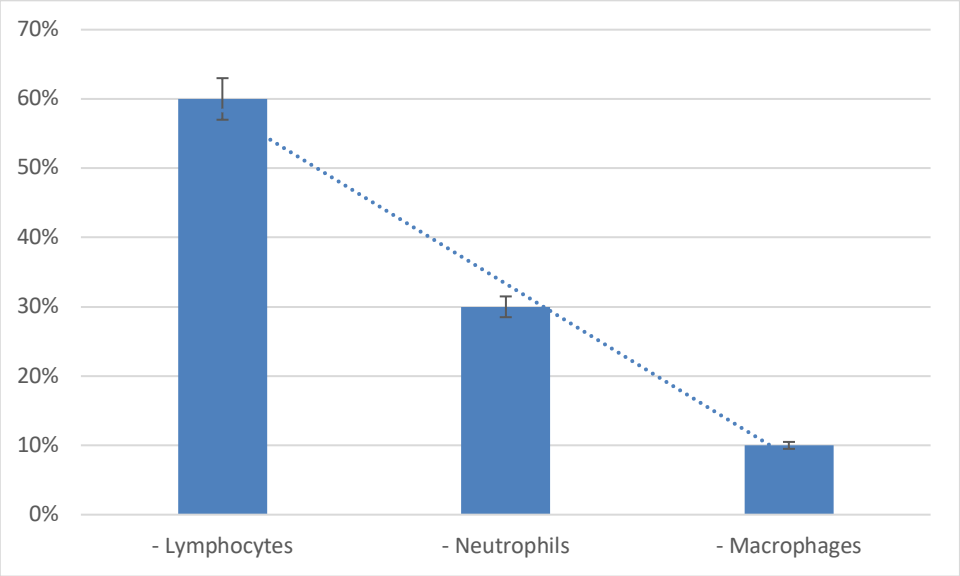


Figure 3. Percentage of Inflammatory infiltrate found in UTI in histology

The treatment outcomes were predominantly favorable, with 90% of patients showing a positive response. Symptoms resolved within 7-10 days for most cases, indicating an effective therapeutic intervention. However, 10% of patients required hospitalization, suggesting the severity of their condition or the need for more intensive management strategies.

Table 3: Primary outcomes

Treatment Outcome	Percentage (%)
Favorable response	90%
Resolution of symptoms	7-10 days
Hospitalization required	10%

DISCUSSION

The findings of this study reveal a high prevalence of chronic urothelial inflammation among women with UTI, with histopathological analysis showing a predominance of lymphocytic infiltrate. These results are consistent with previous studies highlighting the role of chronic inflammation in the pathogenesis of UTI-related symptoms. The observed microbiological profile, with Escherichia coli being the most prevalent pathogen, aligns with established literature on the etiology of UTIs in women (Jagtap et al., 2021). However, the presence of other pathogens such as Klebsiella

pneumoniae and Enterococcus faecalis underscores the importance of comprehensive microbiological evaluation in UTI management. The bladder urothelium is assumed not just to serve as the protective barrier preventing erroneous signaling on bladder stretching and noxious stimuli but also as the one that receives these signals (Liu et al., 2023). Another study revealed that the antiproliferative factor secreted by the urothelium established enhanced ML in the cell cultures, modulated cytokines, associated with the augmentation of purinergic signalling, and mediated the increased bladder sensitivity (Velez and Pontari, 2023). As for the second theme, SC found that another study about the apoptotic phenomenon in IC urothelium illustrated that apoptosis was truly possible in patients with IC and indicated that this apoptotic rate was probably modulated by inflammatory processes. Pro-apoptotic signals were found more frequently in the sections of bladder tissues sampled from IC patients (Goubet et al., 2023). This could explain the higher apoptosis levels observed in the bladder urothelium of the patients with IC because inflammatory signals are upregulated. Similarly, in this work, we also confirmed the abnormalities such as inflammation, urothelial apoptosis and barrier dysfunction in the biopsied specimens from ESRD/CKD population, which indicates that there is chance that chronic inflammation might be the essential form of pathophysiology in the bladder of the patients (Martin et al., 2020). As you know, inflammation is a dangerous condition and it is present in most of the patients who are suffering from OAB. The LR-MS of the compared plasma samples of the healthy volunteers, OAB, IC, and UTI differentiated several biomarkers that were markedly elevated in OAB, including the interleukin-4, TNF-α, macrophage inflammatory protein-1β, serum amyloid A and Tie2 which may be useful in distinguishing the OAB from other conditions (Yu et al., 2022). Prolonged neural plasticity by the chronic inflammation and activation of sensory receptors may alter the number and intensity of the sensory afferent activity through additional or reduced antinociceptive activity and leads to bladder oversensitivity or to the provocation of DO. Studies have revealed that the urinary nerve growth factor (NGF) levels in patients with OAB, IC or other bladder oversensitivity have increased, it can be argued that these various LUTDs might have impassable links to the increased bladder sensations.

CONCLUSION

It is concluded that chronic urothelial inflammation is prevalent among women with urinary tract infections (UTIs), characterized by lymphocytic infiltrate and a microbiological profile dominated by Escherichia coli. Despite the effective response to treatment in many cases, the need for hospitalization highlights the complexity of UTI management.

Conflict of Interest

The authors declare no conflict of interest.

Ethical Approval

This study was approved by IRB committee of Shifa International Hospital Islamabad.

Consent for publication

All authors approved manuscript for publication.

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