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Clinicopathological Analysis of Chronic Urothelial Inflammation Associated with UTI in Women

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ABSTRACT

Background and objective: Patients with end-stage renal disease (ESRD) usually have a small bladder capacity and increased bladder sensation. Patients on chronic dialysis usually have lower urinary tract symptoms (LUTS), such as bladder oversensitivity (BO) or difficulty in urination. The basic aim of the study is to analyze the clinicopathological analysis of chronic urothelial inflammation associated with UTI in women. **Material and methods:** This cross sectional study was conducted in Galway University Hospital, Galway, and Republic of Ireland during 1st of January 2015 till June 2020. The sample size was collected through non-probability sampling technique. The data was collected from 100 female patients. Bladder symptoms and lower urinary tract conditions were investigated. The analytical variables included gender, CKD or ESRD, anuria or nonanuria, history of UCC of the bladder, the presence of recurrent UTIs, and clinical symptoms of bladder pain. **Results:** The data was collected from 100 patients. The mean age was 52.5±13.7 years. The analysis of data shows the differences in urodynamic variables between the control subjects and the ESRD/CKD patients. Overall, the ESRD/CKD patients had significantly lower FS, US, and CBC than did the controls. Patients with ESRD/CKD with DU had significantly lower FS, CBC in ESRD/DU patients with BO. **Conclusion:** It is concluded from our study that chronic inflammation, urothelial cell apoptosis and impairment of barrier function of urothelial cells could be the underlying pathophysiology of recurrent UTI in women.

INTRODUCTION

Patients with end-stage renal disease (ESRD) usually have a small bladder capacity and increased bladder sensation. Patients on chronic dialysis usually have lower urinary tract symptoms (LUTS), such as bladder oversensitivity (BO) or difficulty in urination [1]. The prevalence of urinary tract infections (UTIs) and the incidence of urothelial cell carcinoma (UCC) are also higher in patients with ESRD [2]. Among patients with ESRD, the capacity and compliance of the bladder decrease significantly with the duration of dialysis. In one study, abnormal storage function was noted in up to 71% of ESRD patients and bladder outlet obstruction in 51.6%. Vesicoureteral reflux and high postvoid residual (PVR) urine volumes were observed in 110 of 622 (17.5%) and 83 of 62 patients 2 (13.6%), respectively.

Recurrent urinary tract infection (UTI) is a very bothersome and a popular problem in the urogynecology clinical practice. According to the IUGA/ICS joint report on the terminology for female pelvic floor dysfunction, recurrent UTI is defined as at least three symptomatic and medically diagnosed UTI in the previous 12 months. The previous UTI(s) should have resolved prior to a further UTI being diagnosed. Recurrent UTI is one of the most common diagnoses for female pelvic floor dysfunction [3].

Although the bladder capacity increased after kidney transplantation and LUTS remained present in only 31 of 622 of patients (4.9%), patients who did not receive kidney transplants still experienced bothersome bladder symptoms[4]. Patients with end-stage renal disease (ESRD) usually have a small bladder capacity and increased bladder sensation. Patients on chronic dialysis usually have lower urinary tract symptoms (LUTS), such as bladder oversensitivity (BO) or difficulty in urination [5].

The basic aim of the study is to analyze the clinicopathological analysis of chronic urothelial inflammation associated with UTI in women.

MATERIAL AND METHODS

This cross sectional study was conducted in Galway University Hospital, Galway, Republic of Ireland during 1st of January 2015 till June 2020. The sample size was collected through non-probability sampling technique.

Data collection

The data was collected from 100 female patients. Bladder symptoms and lower urinary tract conditions were investigated. The analytical variables included gender, CKD or ESRD, anuria or non anuria, history of UCC of the bladder, the presence of recurrent UTIs, and clinical symptoms of bladder pain. Each patient was informed of the study rationale and procedures and written informed consent was obtained before cystoscopy and bladder biopsy procedures. All experimental methods were performed in accordance with relevant guidelines and regulations. The urinary bladder specimens were immediately fixed in ice cold 4% formaldehyde phosphate buffered saline (PBS) (pH, 7.4) solution for 1 hour. Next, they were rinsed overnight with ice-cold PBS containing 15% sucrose at 4˚C. Then, the specimens were embedded in optimal cutting temperature medium (Miles) and stored at −80˚C in liquid nitrogen.

Statistical analysis

The collected data were analyzed using SPSS software (version 20). The results are presented as a mean with 95% confidence interval limits or standard deviations. The significant value for P <.05 was accepted as statistically significant.

RESULTS

The data was collected from 100 patients. The mean age was 52.5±13.7 years. The analysis of data shows the differences in urodynamic variables between the control subjects and the ESRD/CKD patients. Overall, the ESRD/CKD patients had significantly lower FS, US, and CBC than did the controls. Patients with ESRD/CKD with DU had significantly lower FS, CBC in ESRD/DU patients with BO (table 01).

Table No. 01: Analysis of socio demographical variables of patients and control group

Variable	Controls (n = 100)	ESRD/CKD		
		Total	With DU	With BO
Age (yr)	57.9 ± 11.7	59.1 ± 15.0	54.8 ± 11.1	61.0 ± 16.3
FSF (mL)	180.1 ± 65.8	140.2 ± 94.2	63.5 ± 31.8	154.2 ± 95.6
FS (mL)	322.1 ± 81.7	178.3 ± 136.1	66.3 ± 49.6	206.3 ± 137.3*
US (mL)	403.5 ± 104.0	195 ± 133.9	79.3 ± 62.4*	223.9 ± 132.4*
CBC (mL)	404.8 ± 113	204.5 ± 149.1*	79.3 ± 62.4*	235.8 ± 149.2*
Pdet (cm H_2O)	24.4 ± 15.7	26.9 ± 20.0	10.5 ± 9.19	29.7 ± 20.2
Qmax (mL/sec)	18.2 ± 11.6	11.7 ± 11.3	0	13.7 ± 11.1
PVR (mL)	51.8 ± 84.0	104.8 ± 164.5	95 ± 77.8	106.4 ± 177.3
Volume (mL)	363.9 ± 175.1	145.7 ± 130.1*	3.33 ± 5.77*	181.3 ± 120.9*
Pves (cm H_2O)	32.4 ± 17.1	32.8 ± 20.8	28.5 ± 16.3	33.5 ± 22.0

*P<0.05

Figure 01 shows the infected area in chronic urothelial inflammation in the bladder of patient with CKD.

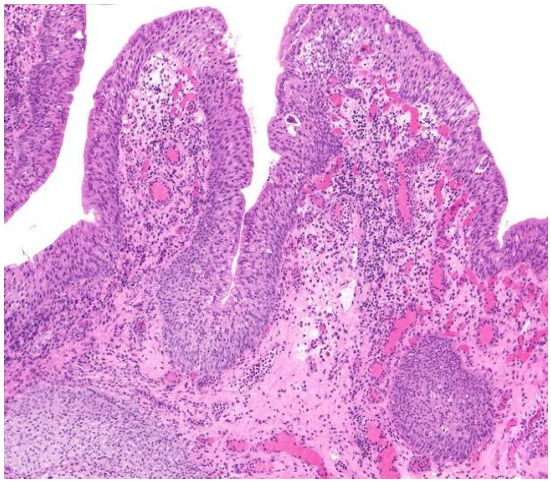

Figure No. 01: Chronic urothelial inflammation in the bladder of patient with CKD

DISCUSSION

One recent study demonstrated localized production of mast cell interleukin-10 resulted in suppressed humoral and cell-mediated responses and bacterial persistence. Tissue-resident mast cells not only orchestrate the early innate immunity during bladder infection, they subsequently play a tissue-specific immunosuppressive role which might have association with the recurrent UTI[6]. This observation might explain the mast cell mediated inflammation and related urothelial dysfunction in recurrent bladder infection [7].

The bladder urothelium is considered not only to act as a barrier, but also to transmit signals of bladder stretching and noxious stimuli. A previous study showed that the anti proliferative factor presented by the urothelium induced increased membrane permeability in cell cultures; regulated the expression of cytokines, which are linked to enhanced purinergic signaling; and mediated increased bladder sensation[8]. Another study revealed that apoptosis was present in the urothelium of patients with IC and showed that it was possibly regulated by inflammatory pathways. Apoptotic signaling molecules were more common in the bladder tissues of IC patients[9]. The increased apoptosis in the bladder urothelium of IC patients could be due to the upregulation of inflammatory signals. In this study, we observed the same patterns of inflammation, urothelial apoptosis, and barrier deficits in bladder samples from ESRD/CKD patients, suggesting that chronic inflammation might be a fundamental form of pathophysiology in the bladders of these patients[10].

Bladder mast cell activation has been reported as a representative pathological finding in a subset of IC patients. Normal basal cell proliferation could be inhibited by chronic inflammation, which might affect apical urothelial function [11]. In this study, the results of TUNEL staining were correlated with those of tryptase staining, indicating that chronic inflammation of the suburothelium was significantly associated with higher levels of urothelial apoptosis in the bladders of patients with ESRD/CKD. These associations demonstrate that inflammation caused increased apoptosis and affected urothelial sensory function in ESRD/CKD patients [12].

RECOMMENDATIONS

We suggest that chronic pain syndrome in the bladders of patients with ESRD/CKD could be related to central nervous system sensitization and sustained abnormalities in or activation of the

sensory afferent nerves in the urinary bladder. Analysis of the functional proteins in the urothelium might help explain the underlying pathophysiology.

CONCLUSION

It is concluded from our study that chronic inflammation, urothelial cell apoptosis and impairment of barrier function of urothelial cells could be the underlying pathophysiology of recurrent UTI in women.

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