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MICROORGANISMS, ANTIBIOTIC RESISTANCE PREDICTION ABOUT POSTOPERATIVE UTI IN TRANSURETHRAL RESECTION SURGERIES OF THE BLADDER

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ABSTRACT

Background: Transurethral resection surgeries of the bladder are a common procedure done in urology. Subjects having asymptomatic bacteriuria before surgery have an increased risk of sepsis and bacteremia. No definitive data exist for antibiotic prophylaxis before these surgeries despite being a common procedure.

Aim: To assess the microorganisms and antibiotic resistance prediction in subjects undergoing transurethral resection surgeries of the bladder and identify the risk factors for the UTI (urinary tract infection) following the procedure.

Methods: In 100 subjects undergoing Transurethral resection surgeries of the bladder, drug-resistance patterns and microbiologic characteristics of isolation frequencies were assessed before and after the surgery. Independent risk factors for UTI were also assessed in these subjects.

Results: 14 positive urine cultures were seen where E. coli was seen in 50% (n=7) subjects, E. faecalis in 28.57% (n=4), P. mirabilis in 7.14% (n=1), and other microorganisms in 21.42% (n=3) subjects respectively before TURBT. Postoperatively, positive urine culture was seen in 11 subjects with E. coli in 45.4% (n=5), E. faecalis in 27.2% (n=3), P. mirabilis in 9.09% (n=1), and others in 18.1% (n=2) subjects respectively. Before surgery, 71.4% (n=5) subjects were resistant to TMP/SMX, ampicillin, and ciprofloxacin, 57.14% (n=4) for Fosfomycin, 42.85% (n=3) for gentamycin, and 14.28% (n=1) for nitrofurantoin. All E. faecalis were resistant to TMP/SMX, and all subjects with P. mirabilis were resistant to TMP/SMX, ampicillin, Fosfomycin, ciprofloxacin, and nitrofurantoin. After TURBT, for E. coli, the resistance was seen for TMP/SMX in 60% (n=3), for ampicillin in 80% (n=4), Fosfomycin in 20% (n=1), for ciprofloxacin in 40% (n=2), gentamycin in 20% (n=1), and for nitrofurantoin in 20% (n=1) subjects respectively

Conclusion: The study concludes that a high UTI prevalence is seen after Transurethral resection surgeries of the bladder. Preoperative positive urine culture was the most common risk factor for UTI following TURB. The most frequently associated uropathogens are E. coli, E. faecalis, and P.

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mirabilis. The most common antibiotic resistance of E. coli is seen in ciprofloxacin and sulfamethoxazole/trimethoprim.

Keywords: Antibiotic resistance, microorganisms, Transurethral resection surgeries of the bladder, UTI

INTRODUCTION

The tenth most common cancer seen globally is bladder cancer. Bladder cancer shows a high global incidence with nearly 549,393 new cases reported in the single year 2018. In the past five years, a very high prevalence of bladder cancer with 1,648,482 cases which ranked bladder cancer to be the sixth most common cancer globally. Also, bladder cancer has a thirteenth place in mortality worldwide with nearly 200,000 deaths caused by bladder cancer alone. Among all the reported genitourinary cancers, 14% of all were bladder cancer.[1]

One of the most common surgical procedures done in bladder cancer cases is TURBT (Transurethral resection of bladder tumor). TURBT is also the main diagnostic and therapeutic tool used in cases of bladder cancer as it helps in the determination of tumor grade and stage as it fulgurates or resects all the tumor visible. The common postoperative complications associated with TURBT are postoperative death, bladder perforation, bleeding, and postoperative infection. Previous literature data have shown an association between increased incidence of bacteremia and UTI (urinary tract infection) the urologic instrumentation.[2]

The postoperative rates of infection usually showed the presence of significant bacteriuria. The current literature data carries limited information concerning the complications associated with Transurethral resection of bladder tumors. The incidence of Transurethral resection of bladder tumor-associated UTI is seen in the range of 18% to 75% in different geographical locations and under different circumstances. A urine culture preoperatively must be done and should get negative results before any surgical intervention is carried out.[3]

Subjects having asymptomatic bacteriuria before the surgical intervention pose a high risk of subjects presenting with sepsis and bacteremia. However, to date, no consensus in the literature exists concerning antibiotic prophylaxis use in Transurethral resection of bladder tumors despite TURBT being the most commonly done surgical procedure.[4,5] The present study aimed to assess the incidence of drug resistance and microorganisms in subjects undergoing Transurethral resection of bladder tumor and to find independent risk factors for postoperative UTI.

MATERIALS AND METHODS

The present retrospective, analytical, and descriptive study was aimed to assess the microorganisms and antibiotic resistance prediction in subjects undergoing transurethral resection surgeries of the bladder and identifying the risk factors for the UTI (urinary tract infection) following the procedure. The study was done after the clearance was given by the concerned Institutional Ethical committee. The study population was recruited from the Department of Urology of the Institute. Written and verbal informed consent was taken from all the subjects before study participation.

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The study included 100 subjects from both genders that underwent TURBT at the Institute. The inclusion criteria for the study were subjects of age more than 18 years, having undergone TURBT in the institute, having preoperative urine culture, and having complete data needed for the study. The exclusion criteria for the study were subjects with incomplete data, incomplete follow-up records, no information on the urine culture, and no informed consent.

The study subjects were divided into two groups where Group I had subjects that reported the UTI in the first 30 days following the surgery and Group II had subjects that presented with no UTI. To assess the UTI presence, a search was done for the PUCs (positive urine cultures) in the first 30 days after the surgical procedure was first done. This was followed by reviewing the follow-up notes to confirm the diagnosis of UTI and initiate the appropriate treatment of UTI.

The data gathered were gathered for all the study subjects including comorbidities, tobacco use, BMI (body mass index), age, and gender. Also, in both groups, infectious characteristics including antibiotic resistance, isolations, and preoperative urine culture were assessed along with the oncologic characteristics including tumor quantity, necrosis, tumor grade, and histopathology reports.

The data gathered were analyzed statistically using SPSS software version 24.0 (IBM Corp., NY, USA) along with the Mann-Whitney U test and Student's t-test. Multivariate and univariate logistic regression analyses were done to assess the risk factors associated with UTI presence. A p-value of <0.05 was taken as statistically significant.

RESULTS

The present retrospective, analytical, and descriptive study was aimed to assess the microorganisms and antibiotic resistance prediction in subjects undergoing transurethral resection surgeries of the bladder and identifying the risk factors for the UTI (urinary tract infection) following the procedure. The study included 100 subjects that met the inclusion criteria. Among 100 subjects, 10 subjects were included in Group I, and 90 subjects were included in Group II. The incidence of UTI in the present study was 10%. The mean age of the study subjects in Group I and II was 70.2±2.4 and 68.4±11.2 years respectively with non-significant differences with p=0.237, and the mean BMI was 26.5±4.9 and 25.5±4.5 kg/m2with p=0.355. There were 60% (n=6) males and 40% (n=4) females in Group I and 80% (n=72) males and 20% (n=18) females in Group II with a non-significant difference (p=0.06). History of tobacco use was positive in 60% (n=6) subjects from Group I and 47.7% (n=43) subjects from Group II which was non-significant with p=0.303. History of diabetes mellitus was positive in 30% (n=3) and 25.5% (n=23) subjects from Group I and II respectively (p=0.54). Hypertension was reported in 60% (n=6) and 47.7% (n=43) subjects from Groups I and II respectively with p=0.303 (Table 1).

The single tumor was seen in 40% (n=4) subjects with positive UTI and 28.8% (n=26) subjects with negative UTI which was non-significant with p=0.114. Necrosis was present in 30% (n=3) and 4.4% (n=4) subjects in Groups I and II respectively which was significantly higher in positive UTI subjects with p=0.001. The high-grade tumor was seen in 70% (n=7) and 52.2% (n=47) subjects from UTI-positive and negative groups respectively showing statistical non-significance

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with p=0.16. Cystitis was higher in UTI-negative subjects at 21.1% (n=19) compared to UTI-positive in 10% (n=1) which was non-significant with p=0.13. Muscle invasive carcinoma was positive in 40% (n=4) subjects with positive UTI which was significantly higher compared to UTI-negative subjects with 14.4% (n=13) subjects (p=0.03). Nonmuscle invasive carcinoma was seen in 50% (n=5) subjects from Group I which was significantly lower compared to 58.8% (n=53) subjects in Group II with p=0.03. Preoperative positive urine culture was significantly higher in positive UTI subjects with 50% (n=5) subjects compared to 10% (n=9) subjects from Group II and p=0.001 (Table 1).

In the univariate analysis, the OR (Odd's ratio) for BMI was 1.03 (0.91-1.15) in UTI-negative and positive subjects with p=0.361. For age, OR was 1.04 (0.96-1.08) which was non-significant with p=0.323. For necrosis, OR was 7.14 (2.05-24.53) which was significant with p=0.002. For high-grade cancer, cystitis, diabetes mellitus, and gender, the results were non-significant with OR of 2.13 (0.75-5.71), 4.62 (0.57-36.11), 1.2 (0.47-4.01), and 2.3 (0.7-6.5) and respective p-values of 0.161, 0.161, 0.523, and 0.05 respectively. For muscle-invasive carcinoma, non-muscle invasive carcinoma, and positive urine culture before TURBT, the OR was 3.12 (1.05-9.24), 0.33 (0.12-0.95), and 8.7 (3.26-6.73) respectively and p=0.03, 0.03, and 0.001 respectively as depicted in Table 2.

Concerning the multivariate analysis, the results were non-significant with OR of 4.74 ((0.88-25.93), 2.27 (0.68-7.68), and 0.46 (0.15-1.52) respectively, and p-values of 0.08, 0.195, and 0.195 respectively. Significant results were seen for positive culture before TURBT with OR and p-value of 7.06 (2.13-23.27) and 0.001 respectively as shown in Table 3.

On assessing the microorganisms and antibiotic resistance in the study subjects, it was seen that 14 positive urine cultures were seen where E. coli was seen in 50% (n=7) subjects, E. faecalis in 28.57% (n=4), P. mirabilis in 7.14% (n=1), and other microorganisms in 21.42% (n=3) subjects respectively before TURBT. Postoperatively, positive urine culture was seen in 11 subjects with E. coli in 45.4% (n=5), E. faecalis in 27.2% (n=3), P. mirabilis in 9.09% (n=1), and others in 18.1% (n=2) subjects respectively. Before surgery, 71.4% (n=5) subjects were resistant to TMP/SMX, ampicillin, and ciprofloxacin, 57.14% (n=4) for Fosfomycin, 42.85% (n=3) for gentamycin, and 14.28% (n=1) for nitrofurantoin. All E. faecalis were resistant to TMP/SMX, and all subjects with P. mirabilis were resistant to TMP/SMX, ampicillin, Fosfomycin, ciprofloxacin, and nitrofurantoin. After TURBT, for E. coli, the resistance was seen for TMP/SMX in 60% (n=3), for ampicillin in 80% (n=4), Fosfomycin in 20% (n=1), for ciprofloxacin in 40% (n=2), gentamycin in 20% (n=1), and for nitrofurantoin in 20% (n=1) subjects respectively (Table 4).

DISCUSSION

The study included 100 subjects that met the inclusion criteria. Among 100 subjects, 10 subjects were included in Group I, and 90 subjects were included in Group II. The incidence of UTI in the present study was 10%. The mean age of the study subjects in Group I and II was 70.2±2.4 and 68.4±11.2 years respectively with non-significant differences with p=0.237, and the mean BMI was 26.5±4.9 and 25.5±4.5 kg/m2with p=0.355. There were 60% (n=6) males and 40% (n=4)

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females in Group I and 80% (n=72) males and 20% (n=18) females in Group II with a non-significant difference (p=0.06). History of tobacco use was positive in 60% (n=6) subjects from Group I and 47.7% (n=43) subjects from Group II which was non-significant with p=0.303. History of diabetes mellitus was positive in 30% (n=3) and 25.5% (n=23) subjects from Group I and II respectively (p=0.54). Hypertension was reported in 60% (n=6) and 47.7% (n=43) subjects from Groups I and II respectively with p=0.303. These results were similar to the studies of Kirkali Z et al[6] in 2005 and Jimenez Rios MA et al[7] in 2011 where authors assessed subjects with demographic data comparable to the present study.

For tumor characteristics, a Single tumor was seen in 40% (n=4) subjects with positive UTI and 28.8% (n=26) subjects with negative UTI which was non-significant with p=0.114. Necrosis was present in 30% (n=3) and 4.4% (n=4) subjects in Groups I and II respectively which was significantly higher in positive UTI subjects with p=0.001. The high-grade tumor was seen in 70% (n=7) and 52.2% (n=47) subjects from UTI-positive and negative groups respectively showing statistical non-significance with p=0.16. Cystitis was higher in UTI-negative subjects at 21.1% (n=19) compared to UTI-positive in 10% (n=1) which was non-significant with p=0.13. Muscle invasive carcinoma was positive in 40% (n=4) subjects with positive UTI which was significantly higher compared to UTI-negative subjects with 14.4% (n=13) subjects (p=0.03). Non-muscle invasive carcinoma was seen in 50% (n=5) subjects from Group I which was significantly lower compared to 58.8% (n=53) subjects in Group II with p=0.03. Preoperative positive urine culture was significantly higher in positive UTI subjects with 50% (n=5) subjects compared to 10% (n=9) subjects from Group II and p=0.001. These results were comparable to the studies of Alsaywid B et al[8] in 2013 and Kohada Y et al[9] in 2019 where authors reported similar tumor characteristics in their study subjects as seen in the present study.

Concerning the univariate analysis, the OR (Odd's ratio) for BMI was 1.03 (0.91-1.15) in UTI-negative and positive subjects with p=0.361. For age, OR was 1.04 (0.96-1.08) which was non-significant with p=0.323. For necrosis, OR was 7.14 (2.05-24.53) which was significant with p=0.002. For high-grade cancer, cystitis, diabetes mellitus, and gender, the results were non-significant with OR of 2.13 (0.75-5.71), 4.62 (0.57-36.11), 1.2 (0.47-4.01), and 2.3 (0.7-6.5) and respective p-values of 0.161, 0.161, 0.523, and 0.05 respectively. For muscle-invasive carcinoma, non-muscle invasive carcinoma, and positive urine culture before TURBT, the OR was 3.12 (1.05-9.24), 0.33 (0.12-0.95), and 8.7 (3.26-6.73) respectively and p=0.03, 0.03, and 0.001 respectively. These results were consistent with the studies of Wada K et al[10] in 2013 and El Basri A et al[11] in 2012 where authors where a significant association was seen for necrosis, positive urine culture before TURBT, a non-invasive carcinoma, and muscle-invasive carcinoma as seen in the present study.

Concerning the multivariate analysis, the results were non-significant with OR of 4.74 ((0.88-25.93), 2.27 (0.68-7.68), and 0.46 (0.15-1.52) respectively, and p-values of 0.08, 0.195, and 0.195 respectively. Significant results were seen for positive culture before TURBT with OR and p-value of 7.06 (2.13-23.27) and 0.001 respectively. These findings were in agreement with the findings

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of Eustace A et al[12] in 2013 and Soave A et al[13] in 2015 where a significant association was seen between positive urine culture before TURBT to postoperative results and outcomes.

It was seen that the microorganisms and antibiotic resistance in the study subjects, it was seen that 14 positive urine cultures were seen where E. coli was seen in 50% (n=7) subjects, E. faecalis in 28.57% (n=4), P. mirabilis in 7.14% (n=1), and other microorganisms in 21.42% (n=3) subjects respectively before TURBT. Postoperatively, positive urine culture was seen in 11 subjects with E. coli in 45.4% (n=5), E. faecalis in 27.2% (n=3), P. mirabilis in 9.09% (n=1), and others in 18.1% (n=2) subjects respectively. Before surgery, 71.4% (n=5) subjects were resistant to TMP/SMX, ampicillin, and ciprofloxacin, 57.14% (n=4) for Fosfomycin, 42.85% (n=3) for gentamycin, and 14.28% (n=1) for nitrofurantoin. All E. faecalis were resistant to TMP/SMX, and all subjects with P. mirabilis were resistant to TMP/SMX, ampicillin, Fosfomycin, ciprofloxacin, and nitrofurantoin. After TURBT, for E. coli, the resistance was seen for TMP/SMX in 60% (n=3), for ampicillin in 80% (n=4), Fosfomycin in 20% (n=1), for ciprofloxacin in 40% (n=2), gentamycin in 20% (n=1), and for nitrofurantoin in 20% (n=1) subjects respectively. These findings were in line with the studies of Mulvey MA et al[14] in 2000 and Garza-Montufar ME et al[15] in 2018 where authors reported antibiotic resistance of E. col following TURBT to trimethoprim, ampicillin, and Sulfamethoxazole as seen in the present study.

CONCLUSION

Considering its limitations, the present study concludes that a high UTI prevalence is seen after Transurethral resection surgeries of the bladder. Preoperative positive urine culture was the most common risk factor for UTI following TURB. The most frequently associated uropathogens are E. coli, E. faecalis, and P. mirabilis. The most common antibiotic resistance of E. coli is seen in ciprofloxacin and sulfamethoxazole/trimethoprim.

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TABLES

Characteristics	**Positive UTI**		**Negative UTI**		**p-value**
	Number (n=10)	**Percentage (%)**	**Number (n=90)**	**Percentage (%)**	
Mean age (years)	70.2±2.4		68.4±11.2		0.237
BMI (kg/m2)	26.5±4.9		25.5±4.5		0.355
Gender					
Males	6	60	72	80	0.06
Females	4	40	18	20	
Single tumor	4	40	26	28.8	0.114
Necrosis presence	3	30	4	4.4	**0.001**
High-grade tumor	7	70	47	52.2	0.16
Cystitis	1	10	19	21.1	0.13

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Muscle-invasive carcinoma	4	40	13	14.4	**0.03**
Non-muscle invasive carcinoma	5	50	53	58.8	**0.03**
Positive urine culture before TURBT					
Yes	5	50	9	10	**0.001**
No	5	50	81	90	
Hypertension					
Yes	6	60	43	47.7	0.303
No	4	40	47	52.2	
Diabetes mellitus					
Yes	3	30	23	25.5	0.54
No	7	70	67	74.4	
Tobacco use					
Yes	6	60	58	64.4	0.654
No	4	40	32	35.5	

Table 1: Demographic and disease characteristics of the study subjects

Variable	**Total (n)**	**Negative UTI**		**Positive UTI**		**OR**	**p-value**
		N=90	**%**	**N=10**	**%**		
Mean BMI (kg.m2)	100	25.5±2.44		26.5±1.86		1.03 (0.91-1.15)	0.361
Mean age (years)	100	68.4±11.2		70.2±2.4		1.04 (0.96-1.08)	0.323
Necrosis							
Yes	7	4	4.44	3	30	7.14 (2.05-24.53)	**0.002**
No	93	86	95.5	7	70		
High-grade cancer							
Yes	54	47	52.2	7	70	2.13 (0.75-5.71)	0.161
No	46	43	47.7	3	30		
Cystitis							
Yes	20	19	21.1	1	10	4.62 (0.57-36.11)	0.161
No	80	71	78.8	9	90		
Muscle-invasive carcinoma							
Yes	17	13	14.4	4	40	3.12 (1.05-9.24)	**0.03**
No	83	77	85.5	6	60		
Non-muscle invasive carcinoma							
Yes	58	54	60	4	40	0.33 (0.12-0.95)	**0.03**
No	42	36	40	6	60		
Positive urine culture before TURBT							
Yes	14	9	10	5	50	8.7 (3.26-6.73)	**0.001**

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No	86	81	90	5	50		
Diabetes mellitus							
Yes	26	23	25.5	3	30	1.2 (0.47-4.01)	0.523
No	60	51	56.6	9	90		
Not known	4	3	3.33	1	10		
Gender							
Female	22	18	20	4	40	2.3 (0.7-6.5)	0.05
Male	78	72	80	6	60		

Table 2: Univariate analysis of independent risk factors associated with UTI following TURBT

Variable	**Total (n)**	**Negative UTI**		**Positive UTI**		**OR (95% CI)**	**p-value**
		N=90	**%**	**N=10**	**%**		
Necrosis							
Yes	7	4	4.44	3	30	4.74 ((0.88-25.93)	0.08
No	93	86	95.5	7	70		
Muscle-invasive bladder cancer							
Yes	17	13	14.4	4	40	2.27 (0.68-7.68)	0.195
No	83	77	85.5	6	60		
Non-muscle invasive bladder cancer							
Yes	58	54	60	4	40	0.46 (0.15-1.52)	0.195
No	42	36	40	6	60		
Positive urine culture before TURBT							
Yes	14	9	10	5	50	7.06 (2.13-23.27)	**0.001**
No	86	81	90	5	50		

Table 3: Assessing the independent risk factors associated with UTI following TURBT

Microorganisms	**n (%)**	**TMP/SMX n (%)**	**Ampicillin n (%)**	**Fosfomycin n (%)**	**Ciprofloxacin n (%)**	**Gentamycin n (%)**	**Nitrofurantoin n (%)**
Before TURBT							
E. coli	7	5 (71.4)	5 (71.4)	4 (57.14)	5 (71.4)	3 (42.85)	1 (14.28)
E. faecalis	4	4 (100)	0	1 (25)	1 (25)	1 (25)	1 (25)
P. mirabilis	1	1 (100)	1 (100)	1 (100)	1 (100)	0	1 (100)
Others	3	2 (66.6)	2 (66.6)	3 (100)	1 (33.3)	2 (66.6)	1 (33.3)
After TURBT							

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E. coli	5	3 (60)	4 (80)	1 (20)	2 (40)	1 (20)	1 (20)
E. faecalis	3	3 (100)	0	1 (33.3)	1 (33.3)	1 (33.3)	1 (33.3)
P. mirabilis	1	1 (100)	1 (100)	1 (100)	0	1 (100)	1 (100)
Others	2	1 (50)	2 (100)	2 (100)	0	1 (50)	1 (50)

Table 4: Microorganisms **and drug resistance in study subjects before and after TURBT**

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	Microogranism	n	ESBL	Nitrofurantoin	Gentamicin	Ciprofloxacin	Fosfomycin	Ampicillin	TMP/SMX
Before TURBT	E. Coli	14 (48%)	2 (14%)	2 (14%)	5 (35%)	10 (71%)	7 (50%)	10 (71%)	10 (71%)
	E. Faecalis	7 (24%)	0 (0%)	2 (28%)	1 (14%)	1 (14%)	1 (14%)	0 (0%)	7 (100%)
	P. Mirabilis	2 (7%)	0 (0%)	2 (100%)	0 (0%)	1 (50%)	2 (100%)	1 (50%)	1 (50%)
	Other	6 (21%)	3 (50%)	2 (33%)	4 (66%)	1 (16%)	6 (100%)	3 (50%)	4 (66%)