Original Article

Peri-operative antibiotic usage during endourological surgery: A multi-institutional, national-level, cross-sectional audit of prevalent practice pattern in India

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ABSTRACT

Introduction: Antibiotic use during endourological procedures is often discordant from the reported guidelines, despite the potential risks of antibiotic resistance, adverse effects, and health-care costs. A nationwide audit was conducted, with the support of the Urological Society of India, to ascertain the current antibiotic prescription practices for the endourological procedures and the reasons associated with them.

Methods: A multi-institutional, national-level, cross-sectional audit analyzing elective endourological procedures was performed. The data regarding the disease profile; risk factors for infectious complications; urine culture; pre-, per-, and post-operative antibiotic use; additional antibiotic use; and patient demographics were collected in a standardized pro forma. Reasons for prescribing antibiotics divergent from the guideline recommendations were also noted. Any infectious complication that necessitated the antibiotic use was also noted prospectively up to 1 month. All the data were entered into a single centralized and customized online portal on a real-time basis.

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Results: One thousand five hundred and thirty-eight cases were recruited from 20 hospitals. A single-dose prophylaxis was prescribed in only 319 (20.7%) of the cases, and the majority received a multi-day prophylaxis. A combination of two or more antibiotics was prescribed as the prophylaxis in 51% of the cases. One thousand three hundred and fifty-six (88.2%) cases were continued on a long-duration prophylaxis after the discharge, with 1191 (77.4%) receiving it for > 3 days. One thousand one hundred and sixty (75.4%) cases received a guideline-discordant prophylaxis solely on the basis of the surgeon's or institution's protocol, rather than any specific case based need. Ninety eight (6.4%) cases developed postoperative urinary tract infection.
Conclusions: Multi-dose, combination and post-discharge antibiotic prophylaxis for endourological surgeries is highly prevalent in India. This audit highlights the huge potential to reduce such guideline-discordant overuse of antibiotics during the endourological procedures.

INTRODUCTION

Antibiotic prescription protocols for the endourological procedures varies across the hospitals in India, despite the availability of a multitude of guidelines recommending a single-dose prophylaxis for the most of the endourological procedures.[1-4] Several factors contribute to this non-adherence to the guidelines including the apprehension of sepsis, a lack of available data and guidelines from the Indian patients, and unique surgical factors such as endourological flora, use of irrigation fluid, stents, and catheters. Antibiotics are over prescribed in up to 50% of the patients undergoing common urological procedures.[5] Evidence suggests that an overuse, beyond the standard recommendation, not only promotes antibiotic resistance and adds to the cost but also exposes the patient to an increased risk of other infections.[5]

This nation-wide audit was conducted with the support of the Urological Society of India (USI), with an aim to document the current antibiotic prescription patterns for the common endourological procedures (cystoscopy, transurethral resection of prostate [TURP], transurethral resection of bladder tumor [TURBT], ureteroscopy [URS], and percutaneous nephrolithotomy [PCNL]). The secondary objectives were to evaluate the factors that drive the antibiotic prescription and to evaluate the incidence of perioperative infections. Such data are a step towards antibiotic stewardship and shall also serve as a baseline to prepare the region-specific guidelines.

MATERIALS AND METHODS

A multi-institutional, national-level, cross-sectional audit was undertaken from April to July 2022. Any urological center with a qualified urologist performing ≥30 endourology cases over a period of 3 months was eligible to enroll. The audit was primarily approved through the local ethics committee vide IEC-812/2021, and then subsequently approved at the each individual participating center.

All consecutive cases of elective cystoscopy, TURP, TURBT, URS, or PCNL were eligible for inclusion. Exclusion criteria included any complication during the surgery requiring the use of means other than the endourological methods; immune-deficiency disorder; cardiac valve implant or risk of infective endocarditis; neurourological diseases necessitating the use of catheters; and, bilateral upper tract procedure. Data regarding the pre-, per-, and post-operative antibiotic use, patient demographics, and the disease profile were collected in a standardized pro forma. The use of any antibiotic, beyond a single perioperative prophylactic dose, was noted along with the reasons for the same. Any infectious complication (febrile illness, pyelonephritis, genital infection, sepsis, and intensive care unit [ICU] admission) requiring the use of antibiotics was prospectively recorded up to 1 month after the surgery and was taken as a surrogate definition of clinical post-operative urinary tract infection (UTI). All the data were entered onto a single centralized and customized online portal on a real-time basis.

Statistical analysis

Descriptive analysis was performed for the demographic and clinical data. The groups with and without infection were compared using the Chi-square analysis for the categorical variables, and the Fisher's exact test was used if the cell values were <5, whereas the one-way ANOVA was utilized for the continuous variables. All the statistical analyses were performed using the Statistical Package for Social Scientists version 25.0 (SPSS Inc., Chicago, IL, United States).

RESULTS

Twenty hospitals across India participated in the study, including 10 from North, 6 from South, 3 from East, and 1 from West Zone as per the USI jurisdiction. Thirteen were government teaching hospitals, 5 were private teaching hospitals, 1 was corporate hospital, and 1 was a single surgeon center. One thousand five hundred and thirty-eight cases were recruited, with an average of 77 ± 71 (range: 6–315) cases per center. Six hundred ninety-eight, 694, 121, and 25 cases were from North, South, East, and West zones, respectively [Table 1]. These were performed by 36 surgeons with a postdoctoral practice experience of <5, 5–15 and >15 years in 9, 13, and 14 surgeons, respectively.

Table 1: Distribution of surgical cases across different geographical zones as per the jurisdiction of Urological Society of India

Procedure type	North	South	East	West	Total, *n* (%)
Cystoscopy	57	48	2	2	109 (7.1)
TURBT	148	29	5	1	183 (11.9)
TURP	117	106	11	5	239 (15.5)
URS	145	275	43	10	473 (30.7)
PCNL	228	235	60	6	529 (34.4)
Data missing	3	1	0	1	5 (0.3)
Total, *n* (%)	698 (45.4)	694 (45.1)	121 (7.9)	25 (1.6)	1538

TURBT=Transurethral resection of bladder tumor, TURP=Transurethral resection of prostate, URS=Ureteroscopy, PCNL=Percutaneous nephrolithotomy

Patient demographics, procedure, and preoperative culture details are provided in Table 2. PCNL and URS constituted 65.1% of the cases.

Preoperative culture and urinary tract infection

Urine culture within 1 week of the surgery was not available for 19.3% of the patients. Two hundred (13%) cases had significant bacterial counts (>10^5 cfu/ml) on the urine culture. *Escherichia coli* (59%) and *Klebsiella* spp. (19.5%) were the most common organisms isolated from the positive cultures.

Overall, postoperative UTI requiring additional antibiotic (s) was reported in 98 (6.4%) cases. The rate of UTI was 10.5% (21/200), if the preoperative culture was positive. Detailed results regarding the rate of UTI stratified as per the procedure and the antibiotic prophylaxis are provided in Table 3.

Preoperative antibiotic use and urinary tract infection

Two hundred cases had a history of antibiotic use within 3 months of the surgery. Two hundred and seventy-four patients were treated with antibiotics immediately preceding the surgery. Table 4 indicates the practice patterns for antibiotic use vis-à-vis urine culture. The rate of UTI was significantly higher in the cases where preoperative antibiotics were administered. Twenty-seven different antibiotics were prescribed and piperacillin + tazobactam was the most common (in 44 cases). Other high-end antibiotics such as cefoperazone + sulbactam, cefixime + clavulanate, cefpodoxime + clavulanate, ceftazidime + tazobactam, ceftazidime + avibactam, ertapenem, faropenem, imipenem, meropenem, and vancomycin were prescribed in additional 112 cases. Preoperative antibiotics were prescribed for a median of 3.5 (mode: 1, range: 1 - >10) days. In 200/274 (73%) cases, the same antibiotic was continued as the peroperative prophylaxis.

The proportion of *Pseudomonas*, *Klebsiella* and *Proteus* spp. taken collectively as the cultured bacteria in the groups with insignificant and significant bacterial counts was 4/28 and 61/200, respectively. After censoring the data of cases that grew these strongly uropathogenic bacteria, the rate of UTI was still consistently higher in those who received the preoperative antibiotics [Table 4].

Peroperative antibiotic use and urinary tract infection

98.3% of the patients were prescribed peroperative prophylaxis. Cefoperazone + sulbactam (41%) was the most common antibiotic followed by ceftriaxone (26%) and piperacillin + tazobactam (8%). A single dose was prescribed in 319 (20.7%) cases, and the other prescribed protocols were 1, 2, 3, or ≥3 days in 20.1%, 18.4%, 24.1%, and 10.9% patients, respectively. An additional antibiotic was prescribed in 788 (51.2%) of the cases. Amikacin was the most common second antibiotic and was prescribed in 693 (45.1%) and was most frequently (26.5%) prescribed as a single dose. However, this additional antibiotic was also continued for 1, 2, 3, or >3 days in 51 (3.3%), 84 (5.5%), 160 (10.4%), and 48 (3.1%) cases, respectively.

Postoperative UTI rates were significantly lower in the patients who received a short duration (1, 2 or 3 days) of per-operative prophylaxis as compared to those who received a single-dose antibiotic [Table 3]. However, when compared with the cases who received >3 days' prophylaxis, the difference was not significant.

Postoperative antibiotic use and urinary tract infection

One thousand three hundred and fifty-six (88.2%) patients were prescribed antibiotics as continued prophylaxis on discharge. For this purpose, oral cephalosporins with or without beta-lactamase inhibitors were the most commonly prescribed antibiotics in 855 (55.6%) followed by fluoroquinolones in 325 (21.1%) and faropenem in 110 (7.1%) cases. 1191 (77.4%) cases received such prophylaxis for > 3 days' duration. The presence of comorbidity or any other predisposing risk factor was not the reason for such a prophylaxis, since 55.1% of the patients who underwent cystoscopy, 26.2% of the TURBT, 30.5% of the TURP, 50.3% of the URS, and 31.9% of the patients who underwent PCNL had no underlying pre-, per- or post-operative predisposing risk factor, by the strictest definition [Supplementary Table 1].

Reasons for antibiotic use other than single-dose prophylaxis

One thousand one hundred and sixty (75.4%) cases received more than the recommended single dose of prophylaxis solely on the basis of surgeon's or institution's protocol. The presence of postoperative stent or nephrostomy

Table 2: Patient demography and pre-operative urine culture details

Parameter	*n* (%)
Number of patients	*n*=1538
Age (years), mean±SD	48.54±17.12
Gender (male/female/others) (percentage males)	1139/398/1 (74.1)
Comorbid illness/predisposing factors	
None	1115 (72.5)
DM	261 (16.9)
Hypothyroidism	27 (1.8)
CKD	56 (3.6)
Hydroureteronephrosis	106 (6.9)
Previous history of recurrent or perioperative UTI/sepsis (even nonurological surgeries)	26 (1.7)
Repeat procedure (within 5 days of first procedure)	3 (0.2)
Urine culture within 1 week of surgery	
Not available	297 (19.3)
Sterile	964 (62.7)
Mixed growth	49 (3.2)
Insignificant counts	28 (1.8)
Significant counts	200 (13)
Name of the bacteria	
Acinetobacter spp.	1 (0.4)
Citrobacter spp.	2 (0.7)
Coagulase-negative *staphylococci*, not specified	1 (0.4)
Enterobacter spp.	1 (0.4)
Enterococcus faecalis	34 (12.3)
Enterococcus spp.	14 (5.1)
Escherichia coli	118 (42.6)
Klebsiella spp.	39 (14.1)
Legionella spp.	1 (0.4)
Other gram-negative bacilli	2 (0.7)
Proteus spp.	4 (1.4)
Pseudomonas spp.	24 (8.7)
Staphylococcus aureus	10 (3.6)
Staphylococcus epidermidis	11 (4)
Staphylococcus spp.	7 (2.5)
Streptococcus pneumoniae	2 (0.7)
Staphylococcus spp.	5 (1.8)
Missing data	1 (0.4)

UTI=Urinary tract infection, DM=Diabetes mellitus, CKD=Chronic kidney disease, SD=Standard deviation

was considered as a significant factor for the continued prophylaxis in 191 (12.4%) cases, while it was considered as the sole factor in only 46 (3%) of these. Suboptimal surgical asepsis or self-cleanliness were the reasons in a minority. Two hundred and seventy-six (17.9%) cases received more than a single-dose of prophylaxis based on multiple (>1) factors. Details of the type and the duration of antibiotic use are provided in Supplementary Table 2.

Procedure details

Individual procedures and the preoperative, intraoperative, and postoperative detailed data, is shown in Supplementary Tables 1 and 2.

DISCUSSION

Multiple factors such as the exposure to Gram-negative *Enterobacteriaceae*; fluid irrigation with the risk of pyelo-venous or pyelo-lymphatic backflow; and, the use of stents, catheters, or nephrostomy before and after the surgery make endourological procedures unique and different from the other surgeries. Hence, the general recommendations for surgical site infections are not directly applicable to the endourological surgeries.[4] However, this lack of applicability has also resulted in the unbridled use of antibiotics for all the endourological surgeries.

Wide variability in the type, duration, and the dose of antibiotics for perioperative prophylaxis has made it difficult to firmly establish its utility. The patient's limited benefit has to be balanced against the adverse drug reactions and serious hazards of antibiotic resistance as well as the health-care costs. Principles of antibiotic prophylaxis necessitate it to be a narrow-spectrum antibiotic being able to prevent infections according to the local antibiogram rather than being a broad-spectrum antibiotic[4] and the second-generation cephalosporin is the most commonly recommended antibiotic across the guidelines.[1-3] Cystoscopy has been categorized as low risk, TURBT and URS as intermediate risk, and TURP and PCNL as high risk for postoperative UTI.[1] Most guidelines strongly recommend a "no use" policy for antibiotics for cystoscopy or TURBT and only a single-dose of prophylaxis for all the other endourological procedures, based on a high-level evidence.[1,3] However, as we found out, the real-life practice is vastly aberrant and almost all the patients were prescribed prophylactic antibiotics and 972 (63.2%) were prescribed a high-end antibiotic (penicillins/cephalosporins with beta-lactamase inhibitors or carbapenems) as the per-operative prophylaxis. More importantly, such a prophylaxis was continued for several days in 73% of the patients and was combined with an additional antibiotic in 51% of them. This additional antibiotic was also continued for several days in as many as 22.3% of the cases, emphasising on the huge unmet need of curtailing the antibiotic use in endourological surgeries, particularly because this practice was primarily driven by the surgeon's or the institution's protocols in more than 75% of the cases, rather than any pressing patient related need.

Preoperative antibiotic use is even more contentious since most of the trials exclude the cases with a positive culture. Many studies suggest that a positive urine culture is a risk factor for UTI.[6,7] However, this risk predisposition has resulted in an assumption that one should achieve a sterile urine status with antibiotics prior to the surgery, as a good clinical practice, without high quality data supporting it. On the contrary, some recent evidence suggests that preoperative antibiotic use, despite reducing the bacteriuria, is an independent risk factor for systemic inflammatory response syndrome (SIRS) and the risk remains high even if one follows a strategy of prolonged preoperative culture-directed antibiotics and confirms a sterile urine on the repeat culture.[8-10] A sterile urinary tract status is more of an assumption than a reality as the uropathogens can

Table 3: Post-operative urinary tract infection rates (as defined by use of antibiotic for clinical urinary tract infection/sepsis within 1 month of procedure) distributed according to various demographic parameters (univariate analysis)

Variable	Postoperative UTI/sepsis, *n* (%)	No postoperative UTI/sepsis, *n* (%)	*P*
Number of patients	98 (6.4)	1440 (93.6)	-
Procedure			
Cystoscopy	12 (11)	97 (89)	-
TURP	18 (7.5)	221 (92.5)	
PCNL	47 (8.9)	482 (91.1)	
TURBT	12 (6.6)	171 (93.4)	
URS	9 (1.9)	464 (98.1)	
Missing data	0	5 (100)	
Immediate preoperative antibiotic use			
Yes	50 (3.2)	224 (14.6)	0.000
No	48 (3.1)	1216 (79.1)	
Preoperative prophylactic antibiotic use (24 data missing)			
None	1 (1)	2 (0.1)	0.001 (single vs. all other doses)
Single dose	33 (33.7)	286 (20.2)	0.000 (single vs. 1 day)
1 day	9 (9.2)	300 (21.2)	0.000 (single vs. 2 day)
2 days	9 (9.2)	274 (19.4)	0.022 (single vs. 3 days)
3 days	21 (21.4)	350 (24.7)	0.583 (single vs. >3 days)
>3 days	20 (20.4)	147 (10.4)	
Missing data	5 (5.1)	57 (4)	
Comorbidities/predisposing factor			
Any	35	388	0.059
None	63	1052	
DM	16	245	0.860 (DM vs. no DM)
CKD	10	46	0.000 (CKD vs. no CKD)
HUN	11	95	0.080 (HUN vs. no HUN)
Previous history of UTI	4	22	0.078 (previous UTI vs. no UTI)
Repeat procedure (within 5 days of 1st procedure)	0	3	
Hypothyroidism	5	22	
Positive urine culture	21	179	0.010
Cystoscopy (*n*=109)	12	97	
Antibiotic used for treating positive culture before the procedure	6	17	0.009
No antibiotic before the procedure	6	80	
No prophylaxis	0	11	0.914
Single dose	5	42	
> single dose	7	42	
Duration data NA	0	2	
TURP (*n*=239)	18	221	
Antibiotic used for treating positive culture before the procedure	11	51	0.000
No antibiotic before the procedure	7	170	
No prophylaxis	0	0	0.005
Single dose	9	47	
> single dose	9	169	
Duration data NA	0	5	
TURBT (*n*=183)	12	171	
Antibiotic used for treating positive culture before the procedure	9	28	0.000
No antibiotic before the procedure	3	143	
No prophylaxis	1	0	0.165
Single dose	1	53	
> single dose	9	97	
Duration data NA	1	19	
Antibiotic data NA	0	2	
URS (*n*=473)	9	464	
Antibiotic used for treating positive culture before the procedure	3	36	0.005
No antibiotic before the procedure	6	428	
No prophylaxis	0	0	0.113
Single dose	2	36	
> single dose	6	408	
Duration data NA	1	12	
Antibiotic data NA	0	8	
PCNL (*n*=529)	47	482	
Antibiotic used for treating positive culture before the procedure	21	91	0.000
No antibiotic before the procedure	26	391	

Contd...

Table 3: Contd...

Variable	Postoperative UTI/sepsis, *n* (%)	No postoperative UTI/sepsis, *n* (%)	*P*
No prophylaxis	0	0	0.122
Single dose	16	115	
> single dose	28	343	
Duration data NA	3	19	
Antibiotic data NA	0	5	

UTI=Urinary tract infection, TURP=Transurethral resection of prostate, TURBT=Transurethral resection of bladder tumor, URS=Ureteroscopy, PCNL=Percutaneous nephrolithotomy, NA=Not available, DM=Diabetes mellitus, CKD=Chronic kidney disease, HUN=Hydro/ureteronephrosis

Table 4: Practice pattern for antibiotic use before the surgery, based on urine culture and corresponding UTI rates

Pre-operative antibiotic use	Urine culture					Total
	Not available	Sterile	Mixed growth	Insignificant growth	Significant growth	
A. Grid of practice pattern for antibiotic use before the surgery, based on urine culture						
Antibiotic used before procedure, *n* (%)	15 - UTI-2 (13.3)	71 - UTI-14 (19.7)	27 UP-1 UTI-10 (37)	22 UP-4 UTI-5 (22.7)	139 UP-44 UTI-19 (13.7)	274 UP-49 UTI-50 (18.2)
Antibiotic not used before procedure, *n* (%)	282 - UTI-9 (3.2)	893 - UTI-37 (4.1)	22 UP-0 UTI-0	6 UP-0 UTI-0	61 UP-17 UTI-2 (3.3)	1264 UP-17 UTI-48 (3.8)
Total	297	964	49	28	200	1538
P value for difference in UTI rate	0.042	0.000	0.001	0.553	0.025	0.000
B. Practice pattern for antibiotic use, excluding cases which grew strongly uropathogenic bacteria on preoperative urine culture						
Antibiotic used before procedure, *n* (%)	15 UTI-2 (13.3)	71 UTI-14 (19.7)	26 UTI-10 (38.5)	18 UTI-5 (27.8)	95 UTI-9 (9.5)	225 UTI-40 (17.8)
Antibiotic not used before procedure, *n* (%)	282 UTI-9 (3.2)	893 UTI-37 (4.1)	22 UTI-0	6 UTI-0	44 UTI-2 (4.5)	1247 UTI-48 (3.8)
Total	297	964	48	24	200	1472
P	0.042	0.000	0.000	0.280	0.316	0.000

Corresponding number of strongly UP bacteria (*Pseudomonas, Klebsiella, and Proteus* spp) and number of UTIs in respective groups are given in parentheses. UP=Uropathogenic, UTIs=Urinary tract infections

be demonstrated in the urinary tract using more potent methods, even when the urine culture is sterile by the standard methods.[11] Stones and biofilms also harbor bacteria shielded from the impact of antibiotics which may get released into the urinary tract during the surgery.[12] The rate of SIRS has also been shown to remain high, despite the intensive perioperative prophylaxis, in cases with a positive urine culture as compared to those with a negative culture.[8] Furthermore, at present, there are no data to suggest that a single dose, 1, 3-, or a 5-day therapy is superior over the other in this setting. Therefore, the use of preoperative antibiotics, with the sole intention of achieving a sterile urine status prior to surgery requires further rigorous evaluation before it can be recommended as a standard policy. Currently, such an approach remains highly driven by the institution's or the individual's perception bias rather than the scientific evidence. We found that the practice patterns of treating the preoperative asymptomatic bacteriuria is highly variable with as many as 30.5% of the cases being prescribed no preoperative antibiotic. Interestingly, a significantly higher rate of UTI was noted in patients who received preoperative antibiotics as compared to those who did not, irrespective of whether the preoperative culture was mixed, insignificant growth, or significant growth. A *post hoc* power analysis showed a 62.3% power keeping the alpha error at 0.05, for this finding. While one may argue for the impact of confounders such as hydronephrosis, comorbidities, type of instruments, sterilization methods, and external tubes on this finding, a higher UTI rate was consistently found across all the individual procedure types as well [Table 2]. This important finding raises a strong doubt on the general practice of treating preoperative asymptomatic bacteriuria prior to all the types of endourological procedures, pending specifically designed studies. Prolonged antibiotic use may also select out more resistant bacteria, alter the normal microbiome of the urinary tract, and predispose to fungal infections, besides its side effects.

Antibiotics after the discharge is another major component of antibiotic use that remains in vogue despite no scientific evidence to suggest its efficacy. An overwhelming 88.2% of the cases received antibiotics at discharge, with 77.4% receiving it for >3 days' duration, clearly indicating overuse, since such a practice is not recommended by any of the guidelines. A recent meta-analysis comparing single versus extended (pre- or post-operative) doses of antibiotics after PCNL did not find an overall difference in the rate of postoperative fever[13] or SIRS. However, considering only the high-risk cases (large stone burden, hydronephrosis, history of UTI, and infected staghorn stone), extended antibiotic use was associated with a lower rate of SIRS when compared to a single dose antibiotic ($P < 0.0001$, odds ratio = 3.53).

On a broader view, these high-risk cases comprised only 27.7% (337/1218) of the cases in this meta-analysis. Further, the heterogeneity of data in the terms of defining high-risk and the type or duration of extended antibiotic use makes it difficult to apply these findings to the general population. Nonetheless, the prevalent practice of aggressive antibiotic use over prolonged periods in post-discharge settings, especially when the majority are low-risk cases, warrants a change. Such a use should be highly discouraged and a policy of "No antibiotic prescription" at the discharge should be firmly adopted unless absolutely indicated.

Cystoscopy has < 5% risk of symptomatic UTI and < 2% risk of systemic UTI as per a recent Cochrane review.[14] Therefore, the potential marginal benefit to be gained by the routine use of prophylactic antibiotics prior to cystoscopy is highly questionable. Many randomized trials show a similar rate of systemic UTI with or without antibiotic prophylaxis[1,3], however, on the other hand, there is significant risk of new-onset bacterial resistance (Risk Ratio =1.73 [1.04–2.87], $P = 0.03$) with the use of antibiotic prophylaxis.[14] Hence, the guidelines discourage prophylactic antibiotics for cystoscopy. Our audit also did not find a significant difference in the rate of 30-day postprocedure UTI after cystoscopy. As discussed previously, preoperative antibiotics prescribed to treat asymptomatic bacteriuria based on the urine culture reports, were found to be detrimental with significantly higher chances of UTI in those who received them. This finding corroborates with the recent evidence from other well-conducted clinical studies[10] and calls for a radical change in the antibiotic prophylaxis protocol for cystoscopy, regardless of the presence of predisposing factors for the development of infection.

TURBT as a procedure is more invasive than diagnostic cystoscopy. However, similar to cystoscopy, prophylactic antibiotics have not been shown to improve the postoperative UTI rates.[15] The use of antibiotic prophylaxis is controversial even in the presence of presumed risk factors, because none of the risk factors (such as age >75 years, indwelling catheter, past pelvic radiotherapy, preoperative hospitalization, positive culture, pyuria, or tumor size) have been consistently shown to predict post-operative UTI across all the studies. We also did not find a difference in the rate of UTI between the different durations of prophylaxis used for TURBT. The cohort that received preoperative antibiotic had a higher incidence of UTI, emphasising that the practice of treating asymptomatic bacteriuria prior to TURBT should be strongly discouraged.

The results for URS and PCNL were similar to those for cystoscopy and TURBT in our audit. The rate of UTI was similar between those who received a single versus more than a single dose of prophylaxis. On the contrary, preoperative antibiotic use was associated with higher postoperative UTI rates. As discussed previously, in a recent meta-analysis, extended prophylaxis was not superior to the standard one when comparing the rate of postoperative fever or SIRS in the patients undergoing PCNL.[13] Potretzke *et al*. evaluated high risk patients (history of previous UTI, hydronephrosis, or stone size ≥2 cm) with sterile urine culture undergoing PCNL under a 7 days, 2 days, or no preoperative antibiotic prophylaxis and found no difference in the rate of SIRS.[16] The rate of SIRS remains high in cases with positive urine culture, as compared to those with negative urine cultures, despite intensive perioperative prophylaxis.[8] Similarly for URS, several studies have demonstrated that preoperative antibiotic use does not reduce the postoperative UTI and fever rates[17] and continued prophylaxis after the discharge does not improve the 30-day UTI rate (2.9% vs. 3.6%, $P = 0.5$).[18,19]

Unlike the other groups in our audit, more than a single-dose antibiotic prophylaxis (5.1% vs. 16.1%, $P = 0.005$) was associated with a reduced rate of UTI in the TURP cohort. This discrepancy may be explained by the high prevalence of risk factors such as the presence of indwelling catheter (59%) and previous UTI (23%). In a systematic review published in 2009, the use of prophylactic antibiotics resulted in a relative risk reduction by 0.51 (confidence intervals: 0.27–0.96) for sepsis when compared to a placebo. However, the absolute risk reduction was only 2% (3.4%–1.4%), and the number needed to treat was 50.[20] Similar to the other surgical groups, TURP group also showed a significantly increased risk of UTI with the use of preoperative antibiotics. This trend was consistent across all the types of endourological surgeries.

The unnecessary, excessive, and guideline-discordant use of antibiotics is a global phenomenon[5,21] and needs concerted efforts at a global level. It is our view, that medico-legal implications on the account of UTI/sepsis may be a major factor driving such an irrational use, as systemic sepsis occurs in a minority and is salvageable with minimal sequelae in the majority.[22,23] Suboptimal surgical asepsis including instrument sterilization/disinfection was reported as a reason for excess antibiotic use in only 9/1538 cases. Most available studies, guidelines, and reviews are also cognizant of the practice of high-level disinfection of the equipment as against the preferred sterilization.[1-4,24] Thus, developing a predictive factor-based strategy is the need of the hour.[25] Auditing the practice patterns, identifying the reasons for excess use, and a focused redressal of these reasons, besides well-conducted clinical studies on the topic, is the only way forward to overcome this menace. Guidelines with due clarity regarding the use of antibiotics in pre-, per-, and post-operative settings, spreading awareness about stewardship, recommending insurance reimbursement for only a single-dose prophylaxis, ensuring antibiotic stewardship as an essential component for hospital accreditation, are the other possible steps in this direction. Till then, it would be helpful to understand the concept of prophylaxis as the prescription of a single dose lower end antibiotic, unless strongly indicated otherwise, and that the antibiotic prophylaxis at the discharge after an uneventful surgery should be discontinued.

The main strengths of this audit are prospective data collection, large response rate, and inclusion of all kinds of cases irrespective of the urine culture status or antibiotic regime. There are a few limitations of this audit as well. First, the data accrual and the distribution of the type of surgery were not uniform across all the zones. Second, it could not be firmly confirmed if all the consecutive cases were enrolled or not, which may induce a sampling bias in the representation of a true real-world situation. However, the finding of a very high per- and post-operative antibiotic usage, across all the types of surgeries, negates its possible impact on the assessment of the real-world situation to a large extent. Third, we do not know whether the preoperative antibiotic administration was coupled with a repeat urine culture and the documentation of a sterile urine status or not. Fourthly, we have not looked at the side effects and the cost-benefit analysis of antibiotic use, which is also an important clinical aspect with an impact on the practice patterns. Fifth, the definition of postoperative UTI defined as the "use of antibiotics" as a surrogate may not reflect the true UTI rates, as these patients may often have stent-related symptoms or noninfective inflammation/fever which may be incorrectly treated with antibiotics irrespective of the culture report. However, this definition more closely reflects the real-world practice for the purpose of an audit on the antibiotic use. Sixthly, we do not have the data on the temporal relation between postoperative UTI and prophylaxis. Finally, whether the postoperative UTI lead to sepsis and ICU admission or not remains unknown and may be an important benchmark to compare between the different antibiotic practices since febrile UTIs can be treated with a salvage antibiotic treatment in an overwhelming majority of the cases.

CONCLUSIONS

Overall, our audit showed that the use of antibiotics as multi-dose, combination, and postdischarge prophylaxis for endourological procedures is highly prevalent in India. Such a use is discordant with the available scientific evidence or guideline recommendations. While there is still a long way to go before standardized antibiotic regimen (s) could be recommended, there is a huge potential to reduce the overuse of antibiotics during these procedures.

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Supplementary Table 1: Procedure-wise details of cases

Cystoscopy	*n* (%)
Number of cases	109
Indication	
Check cystoscopy for bladder cancer	34 (31.2)
Diagnostic cystoscopy	74 (67.9)
Hydrodistension	1 (0.01)
History (within 3 months) of instrumentation	19 (17.4)
History (within 3 months) of catheter-free trial	25 (22.9)
History (within 3 months) of UTI requiring antibiotics	17 (15.6)
No risk factor (diabetes, CKD, hydro/ureteronephrosis, hypothyroid, previous history of UTI, repeat procedure within 5 days, any significant growth on preoperative urine culture, history [within 3 months] of instrumentation, history [within 3 months] of catheter-free trial)	60 (55.1)

TURP/laser prostatectomy	*n* (%)
Number of cases	239
Prostate size on ultrasound (cc)	
<30	26 (10.9)
31–60	129 (54)
61–90	60 (25.1)
>90	22 (9.2)
Missing data	2 (0.8)
On indwelling catheter (days)	142 (59.4)
<3	26 (10.9)
4–7	28 (11.7)
>7	88 (36.8)
Postvoid urine volume on ultrasound (cc)	97 (40.6)
<50	24 (10)
51–150	38 (15.9)
151–250	23 (9.6)
>250	12 (5)
History (within 3 months) of instrumentation	31 (13)
History (within 3 months) of catheter-free trial	79 (33.1)
History (within 3 months) of UTI requiring antibiotics	55 (23)
Resection time (excluding cystoscopy time) (min)	
<45	92 (38.5)
46–75	137 (57.3)
>75	9 (3.8)
Missing data	1 (0.4)
Postoperative irrigation time (h)	
<6	32 (13.4)
6–24	162 (67.8)
24–48	26 (10.9)
>48	2 (0.8)
Missing data	17 (7.1)
Postoperative catheterization time (h)	
<24	13 (5.4)
24–48	100 (41.8)
48–72	62 (25.9)
>72	62 (25.9)
Missing data	2 (0.8)
Postoperative TLC (day 1)	
<10,000	138 (57.7)
10,001–15,000	53 (22.2)
15,001–20,000	4 (1.7)
>20,000	2 (0.8)
Not done	22 (9.2)
Missing data	20 (8.4)
Postoperative clot retention requiring bladder wash	4 (1.7)
No risk factor (diabetes, CKD, hydro/ureteronephrosis, hypothyroid, previous history of UTI, repeat procedure within 5 days, any significant growth on preoperative urine culture, preoperative indwelling catheter, history [within 3 months] of instrumentation, history [within 3 months] of catheter-free trial, resection time >75 min, postoperative irrigation time >48 h, postoperative catheter time >72 h, postoperative TLC on day 1 >20,000/mm³, postoperative clot retention)	73 (30.5)

TURBT	*n* (%)
Number of cases	183
Tumor size on ultrasound (cm)	
<1	23 (12.6)
1.1–3	87 (47.5)
3.1–5	56 (30.6)
>5	17 (9.3)
On indwelling catheter (days)	74 (40.5)
<3	30 (16.4)
4–7	23 (12.6)
>7	21 (11.5)
Postvoid urine volume on ultrasound (cc)	
Not known	37 (33.9)
<50	54 (29.5)
51–150	16 (8.7)
151–250	1 (0.5)
>250	1 (0.5)
History (within 3 months) of instrumentation	46 (25.1)
History (within 3 months) of catheter-free trial	41 (22.4)
History (within 3 months) of UTI requiring antibiotics	29 (15.8)
Resection time (excluding cystoscopy time) (min)	
<45	108 (59)
46–7	60 (32.8)
>75	11 (6)
Missing data	4 (2.2)
Postoperative irrigation time (h)	
<6	10 (5.5)
6–24	133 (72.7)
24–48	31 (16.9)
>48	5 (2.7)
Missing data	4 (2.2)
Postoperative catheterization time (h)	
<24	10 (5.5)
24–48	67 (36.6)
48–72	54 (29.5)
>72	47 (25.7)
Missing data	5 (2.7)
Postoperative TLC (day 1)	
Not done	18 (9.8)
<10,000	98 (53.6)
10,001–15,000	36 (19.7)
15,001–20,000	1 (0.5)
>20,000	1 (0.5)
No risk factor (diabetes, CKD, hydro/ureteronephrosis, hypothyroid, previous history of UTI, repeat procedure within 5 days, any significant growth on preoperative urine culture, preoperative indwelling catheter, history [within 3 months] of instrumentation, history [within 3 months] of catheter-free trial, tumor size >5 cm, resection time >75 min, postoperative irrigation time >48 h, postoperative catheter time >72 h, postoperative TLC on day 1 >20,000/mm³, postoperative clot retention)	48 (26.2)

URS	*n* (%)
Number of cases	473
Stone location	
Lower ureter	204 (43.1)
Mid ureter	67 (14.2)
Upper ureter	153 (32.3)
Renal pelvis	27 (5.7)
Calyx	16 (3.4)
Missing data	6 (1.3)
Stone size on imaging (cm)	
<1	279 (59)
1.1–2	178 (37.6)
>2	4 (0.8)
Missing data	12 (2.5)
On urinary diversion	98
JJ stent	96 (20.3)
Percutaneous nephrostomy	2 (0.4)
History (within 3 months) of instrumentation	60 (12.7)
History (within 3 months) of UTI requiring antibiotics	27 (5.7)
Postoperative catheterization time (h)	
<6	9 (1.9)
6–24	345 (72.9)
24–48	61 (12.9)
>48	17 (3.6)
None	11 (2.3)
Missing data	30 (6.3)
Indwelling JJ stent left *in situ*	446 (94.3)
Postoperative TLC (day 1)	
Not done	40 (8.5)
<10,000	291 (61.5)
10,001–15,000	99 (20.9)
15,001–20,000	12 (2.5)
>20,000	1 (0.2)
Residual fragments	46 (9.7)
No risk factor (diabetes, CKD, hydro/ureteronephrosis, hypothyroid, previous history of UTI, repeat procedure within 5 days, any significant growth on preoperative urine culture, stone size >2 cm, preoperative urinary diversion [JJ stent or nephrostomy], history [within 3 months] of instrumentation, history [within 3 months] of catheter-free trial, postoperative catheter time >72 h, postoperative TLC on day 1 >20,000/mm³, postoperative residual fragments)	238 (50.3)

PCNL	*n* (%)
Number of cases	529
Number of tracts used	
1	358 (67.7)
2	142 (26.8)
>2	16 (3)
Missing data	13 (2.5)
Largest tract size (Fr)	
<15	47 (8.9)
15–21	130 (24.6)
21–25	116 (21.9)
>25	214 (40.5)
Missing data	22 (4.2)
Largest stone size on imaging (cm)	
<1	54 (10.2)
1.1–2	271 (51.2)
>2	127 (24)
Partial staghorn	26 (4.9)
Staghorn	48 (9.1)
Missing data	3 (0.6)
On urinary diversion	169
JJ stent	107 (20.2)
Percutaneous nephrostomy	62 (11.7)
History (within 3 months) of instrumentation	66 (12.5)
History (within 3 months) of UTI requiring antibiotics	72 (13.6)
Postoperative catheterization time (h)	
Nil	92 (17.4)
<6	48 (9.1)
6–24	67 (12.7)
24–48	201 (38)
>48	84 (15.9)
Indwelling JJ stent left *in situ*	480 (90.7)
Indwelling percutaneous nephrostomy left *in situ*	251 (47.4)
Postoperative TLC (day 1)	
<10,000	287 (54.3)
10,001–15,000	191 (36.1)
15,001–20,000	25 (4.7)
>20,000	1 (0.2)
Missing data	25 (4.7)
Residual fragments	44 (8.3)
No risk factor (diabetes, CKD, hydro/ureteronephrosis, hypothyroid, previous history of UTI, repeat procedure within 5 days, any significant growth on preoperative urine culture, partial or complete staghorn stone, preoperative urinary diversion [JJ stent or nephrostomy], history [within 3 months] of instrumentation, history [within 3 months] of catheter-free trial, postoperative catheter time >72 h, postoperative TLC on day 1 >20,000/mm³, postoperative residual fragments)	169 (31.9)

CKD=Chronic kidney disease, UTI=Urinary tract infection, TLC=Total leukocyte count, URS=Ureteroscopy, PCNL=Percutaneous nephrolithotomy, TURP=Transurethral resection of prostate, TURBT=Transurethral resection of bladder tumor

Supplementary Table 2: Details of antibiotics used for the cases

Antibiotics used for treating positive culture before procedure	
Number of cases, *n* (%)	274 (17.8)
Name of primary antibiotic	
Aminoglycoside	13
Beta lactams with beta-lactamase inhibitor	44
Carbapenems	43
Cephalosporin	44
Cephalosporin with beta-lactamase inhibitor	69
Fluoroquinolones	12
Others	42
Missing data	7
Duration (days)	
1	72
2	28
3	35
4	14
5	62
6	7
7	38
9	2
>10	14
Stopped when	
>3 days	30
1–3 days prior	14
Continued as perioperative prophylaxis	200
Missing data	27
Antibiotics used for perioperative prophylaxis	
Number of cases, *n* (%)	1518 (98.7)
Name of primary antibiotic	
Aminoglycoside	43
Penicillins with beta-lactamase inhibitor	124
Carbapenems	33
Cephalosporin	473
Cephalosporin with beta lactamase inhibitor	815
Fluoroquinolones	14
Others	7
Missing data	9
Duration	
Single dose	327
1 day	309
2 days	284
3 days	371
>3 days	167
Missing data	60
Additional antibiotics used for perioperative prophylaxis	
Number of cases, *n* (%)	788 (51.2)
Name of antibiotic	
Amikacin	693
Gentamicin	55
Others	34
Missing data	6
Duration	
Single dose	407
1 day	51
2 days	84
3 days	160
>3 days	48
Missing data	38
Antibiotic used for postoperative clinical UTI/sepsis (up to 1 month after surgery)	
Number of cases, *n* (%)	98 (6.4)
Type of antibiotic	
Aminoglycoside	1
Beta lactams with beta lactamase inhibitor	9
Carbapenems	13
Cephalosporin	15
Cephalosporin with beta lactamase inhibitor	16
Fluoroquinolones	2
Others	21
Combination of two or more	7
Missing data	9
Duration	
Single dose	3
1 day	6
2 days	8
3 days	10
>3 days	63
Missing data	8
Antibiotic used for postoperative prophylaxis of UTI after discharge	
Number of cases, *n* (%)	1356 (88.2)
Type of antibiotic	
Beta lactams	6
Carbapenems	121
Cephalosporin	609
Cephalosporin with beta lactamase inhibitor	260
Fluoroquinolones	325
Others	29
Missing data	6
Duration	
Single dose	10
1 day	5
2 days	5
3 days	135
>3 days	1191
Missing data	10
Reasons for antibiotic use	
Reasons for antibiotic use (if used other than prophylactic peri-operative single dose) (multiple options were applicable)	
Not applicable as only single-dose prophylaxis was given	327
Surgeon protocol	583
Institutional protocol	577
Presence of postoperative JJ stent/percutaneous nephrostomy	191
Suboptimal surgical asepsis	9
Suboptimal self-cleanliness by patient/caregiver	2
Preoperative risk factor as deemed by surgeon	
Carcinoma bladder	3
Carcinoma prostate	1
Hepatitis B	1
Forgotten JJ stent	2
Coronary artery disease	7
Hypertension	87
JJ stent *in situ*	203
Percutaneous nephrostomy *in situ*	64
Indwelling catheter	171
Benign prostatic enlargement	29
Pyelonephritis	2
Positive urine culture	200
DM	261
CKD	56
Hydroureteronephrosis	106
Previous history of recurrent or peri-operative UTI/sepsis	26
Repeat procedure (within 5 days of first procedure)	3
Intraoperative risk factor as deemed by a surgeon	
Impacted calculus	15
Infected system/pus	36
Prolonged surgery	2
Hydrothorax	1
Pyelolymphatic absorption	88
Residual stone/fragments	7
Sepsis	2
Postoperative risk factor as deemed by surgeon	
TLC >10,000	228
Postoperative fever	30
Positive urine culture	7
Hepatitis	1
CKD	3
JJ stent kept *in situ*	119
Urosepsis	4
Septic shock	2
Catheter *in situ*	74
Pulmonary edema	1
Pleural effusion	1
Uncontrolled diabetes	1

CKD=Chronic kidney disease, UTI=Urinary tract infection, DM=Diabetes mellitus, TLC=Total leukocyte count