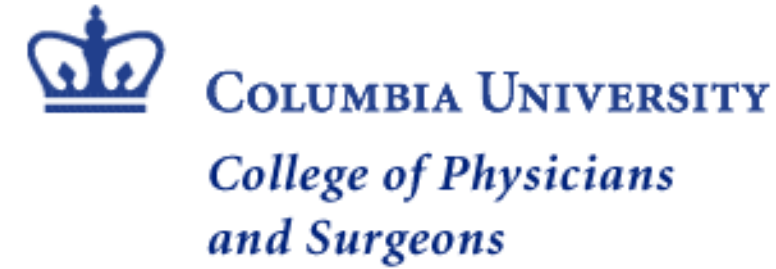


Impact of a Surgical Antimicrobial Prophylaxis Change on the Epidemiology of Urine Isolates in Kidney Transplant Recipients



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Introduction

- Urinary tract infections (UTI) are the most common infection following kidney transplant (KT)
- Asymptomatic bacteriuria after KT has been linked to poor outcomes including progression to symptomatic UTIs, bacteremia and graft rejection
- The full impact of bacteriuria after KT on graft survival remains unclear
- In 2012, the KT surgical antimicrobial prophylaxis protocol at our institution changed from cefazolin to ampicillin-sulbactam in an attempt to decrease early post-KT enterococcal UTIs
- We aimed to assess impact of this change on rates of bacteriuria after KT, the epidemiology of urine isolates, and on graft survival rates

Methods

- Retrospective review of all unique urine isolates within 12 months of transplant for adult KT recipients from 2007-2011 and 2013-2015
- Included first isolate per organism per KT recipient
- KT recipients during protocol transition period of 2012 and multi-organ transplant recipients were excluded
- Multi-drug resistant (MDR): non-susceptible to ≥ 1 agent in ≥ 3 antimicrobial categories
- Extensively-drug resistant (XDR): non-susceptible to ≥ 1 agent in all but ≤ 2 antimicrobial categories

Results

Table 1: Demographics of Kidney Transplant Recipients

	Group 1 (2007-2011)	Group 2 (2013-2015)	p-value
Total Transplants	1156	584	
Median age, yrs (IQR)	53 (41-63)	54 (41-62)	0.92
Male (%)	729 (63.1%)	349 (59.7%)	0.20
Race			
Asian	94 (8.1%)	53 (9.1%)	0.50
Black	186 (16.1%)	119 (20.4%)	0.03
Hispanic	284 (24.6%)	145 (24.8%)	0.95
White	585 (50.6%)	256 (43.8%)	0.01
Other/Unknown	7 (0.6%)	11 (1.9%)	0.03
Donor Type			
Living	598 (51.7%)	305 (52.2%)	0.89
Deceased	558 (48.3%)	279 (47.8%)	0.89
Induction ^a			
Anti-thymocyte globulin	880 (76.7%)	154 (26.4%)	<0.001
Anti-IL-2R antibody ^b	306 (24.6%)	73 (12.5%)	<0.001
Alemtuzumab	5 (0.4%)	362 (62.0%)	<0.001

a: 8 patients in group 1 with unknown induction therapy; 9 patients in group 1 and 2 in group 2 received none of listed induction agents

b: Anti-interleukin-2 receptor antibody including basiliximab or daclizumab

Results

Table 2: Most Frequent Organisms Causing Bacteriuria By Time After Kidney Transplant

	≤ 7 days	≤ 30 days	≤ 6 months	≤ 12 months
Total (n)	83	243	471	552
Group 1	29 <i>E. faecalis</i> (34.9%) 20 <i>E. coli</i> (24.1%) 9 <i>P. aeruginosa</i> (10.8%) 6 <i>K. pneumoniae</i> (7.2%) 19 Other (22.9%)	78 <i>E. coli</i> (32.1%) 59 <i>E. faecalis</i> (24.3%) 29 <i>K. pneumoniae</i> (11.9%) 27 <i>E. faecium</i> (11.1%) 50 Other (20.6%)	151 <i>E. coli</i> (32.1%) 95 <i>E. faecalis</i> (20.2%) 65 <i>K. pneumoniae</i> (13.8%) 58 <i>E. faecium</i> (12.3%) 102 Other (21.7%)	174 <i>E. coli</i> (31.5%) 110 <i>E. faecalis</i> (19.9%) 80 <i>K. pneumoniae</i> (14.5%) 61 <i>E. faecium</i> (11.1%) 127 Other (23.0%)
Total (n)	69	151	255	300
Group 2	29 <i>E. coli</i> (42.0%)^a 20 <i>E. faecalis</i> (29.0%) 7 <i>K. pneumoniae</i> (10.1%) 3 <i>P. aeruginosa</i> (4.3%) 10 Other (14.5%)	54 <i>E. coli</i> (35.8%) 33 <i>E. faecalis</i> (21.9%) 22 <i>K. pneumoniae</i> (14.6%) 16 <i>E. faecium</i> (10.6%) 26 Other (17.2%)	73 <i>E. coli</i> (28.6%) 49 <i>E. faecalis</i> (19.2%) 32 <i>E. faecium</i> (12.5%) 48 Other (18.8%)	86 <i>E. coli</i> (28.7%) 56 <i>E. faecalis</i> (18.7%) 34 <i>E. faecium</i> (11.3%) 61 Other (20.3%)

a: p = 0.03; b: p = 0.01; c: p = 0.02

Figure 1: Resistance Patterns among Gram-negative Isolates

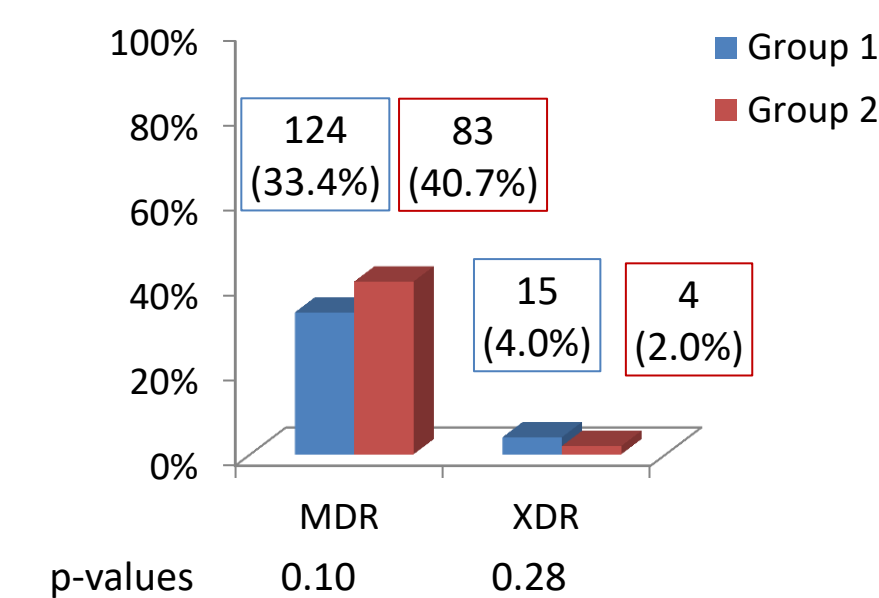


Table 4: Antibiotic Susceptibility of Gram-negative bacilli, *E. coli*, and *K. pneumoniae*

Antibiotic	All Gram-negatives		<i>E. coli</i>		<i>K. pneumoniae</i>	
	1	2	1	2	1	2
Group						
Total (n)	371	204	174	86	80	63
Ampicillin-sulbactam	48.1%	42.3%	41.5%	31.4%	61.1%	60.3%
Cefazolin	59.9%	59.2%	70.4%	64.0%	68.8%	79.4%
Cefepime	91.9%	96.0%	96.2%	97.7%	89.3%	93.7%
Ceftriaxone	82.4%	77.8%	89.2%	86.0%	76.0%	85.7%
Gentamicin	79.7%	82.1%	72.4%	79.1%	88.8%	90.5%
Levofloxacin	66.0%	77.9%^a	50.0%	64.0%^b	75.0%	92.1%^c
Meropenem	95.6%	98.0%	100.0%	98.8%	87.3%	95.2%
Piperacillin-tazobactam	86.1%	81.7%	94.9%	80.2%^d	71.2%	84.1%
TMP-SMX	26.8%	32.8%	17.2%	22.4%	32.5%	31.7%

TMP-SMX: trimethoprim-sulfamethoxazole; a: p = 0.004; b: p = 0.05; c: p = 0.01; d: p = 0.001

Table 3: Antibiotic Susceptibility of *Enterococcus* species

Antibiotic	<i>E. faecalis</i>		<i>E. faecium</i>	
	1	2	1	2
Group				
Total (n)	110	56	61	34
Ampicillin	99.1%	98.2%	0.0%	11.8%^a
Linezolid	99.1%	98.2%	100.0%	97.1%
Vancomycin	93.6%	94.6%	23.0%	29.4%

a: p = 0.01

Table 5: Bacteriuria Rates by Time Post-KT

Time After KT	Group 1	Group 2	p-value
≤ 7 days	65 (5.6%)	57 (9.8%)	0.002
≤ 30 days	207 (17.9%)	131 (22.4%)	0.03
≤ 6 months	340 (29.4%)	180 (30.8%)	0.58
≤ 12 months	375 (32.4%)	196 (33.6%)	0.69

Figure 2: First Episode of Bacteriuria by Time Post-KT

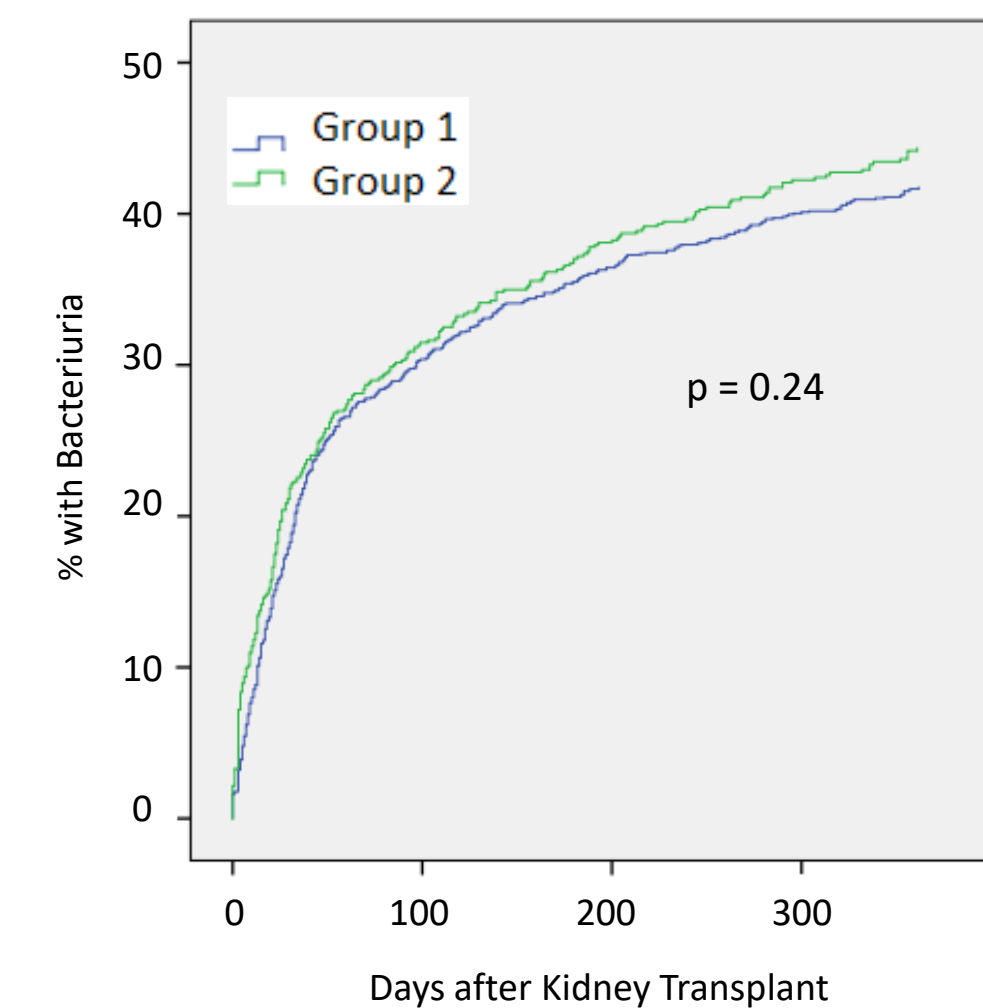
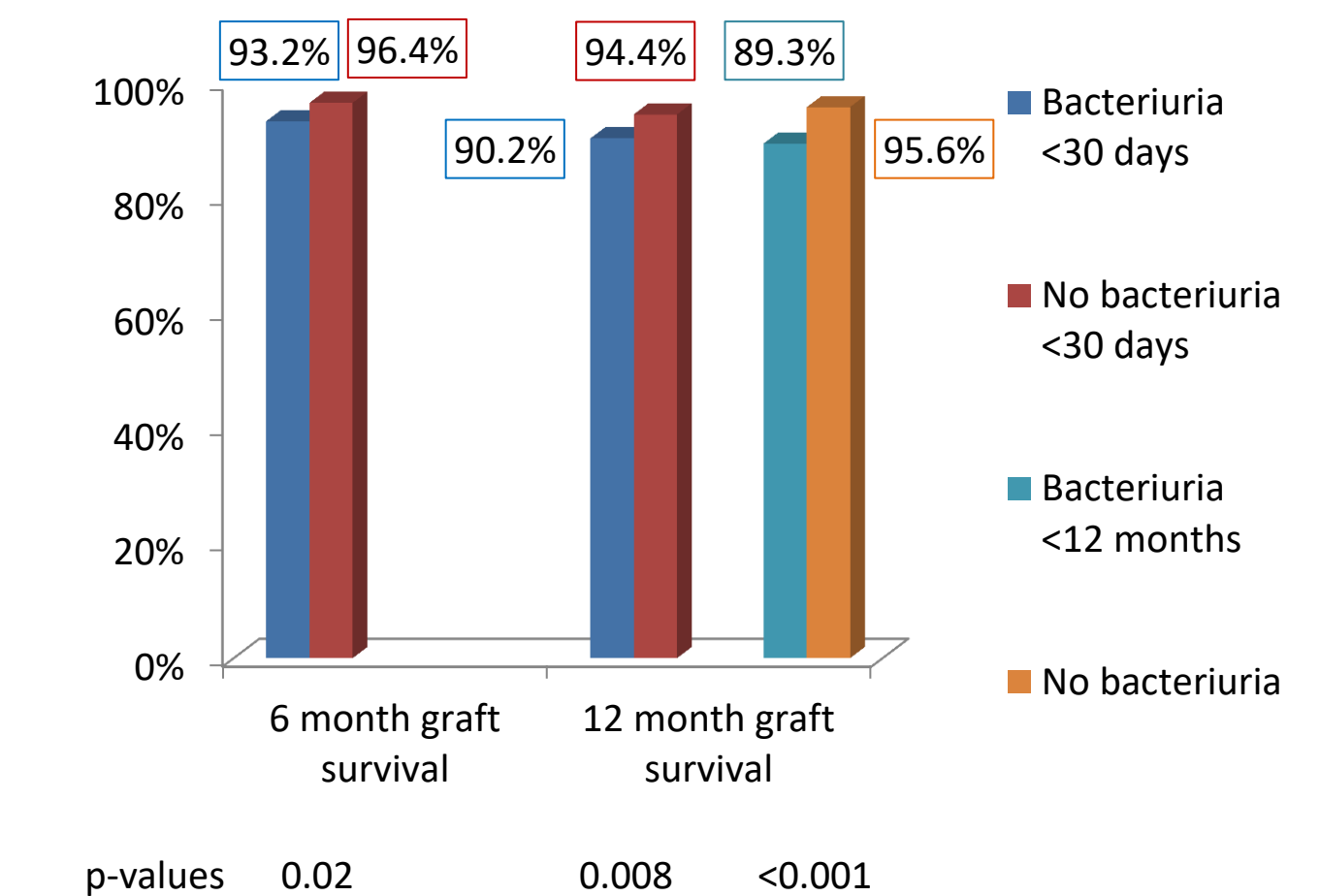


Table 6: Graft Survival Rates Following Kidney Transplant

Graft Survival ^a	Group 1	Group 2	Overall
At 6 months	1105 (95.7%)	560 (95.9%)	1665 (95.7%)
At 12 months	1082 (93.7%)	545 (93.3%)	1627 (93.6%)
Total KTs	1155	584	1739

a: Graft survival data not available for 1 kidney transplant recipient in group 1 lost to follow-up

Figure 3: Graft Survival Rates by Presence of Bacteriuria



Conclusions

- Early bacteriuria both within 7 days and 30 days of KT increased following a change in routine surgical prophylaxis from cefazolin to ampicillin-sulbactam
- *E. coli* remained the most common organism isolated from urine cultures in the first year after KT and surpassed *E. faecalis* in the first week after transplant
- Bacteriuria, both within 30 days and within 12 months of KT, was associated with decreased graft survival, although rates were not significantly different between the time periods
- The potential impact of early bacteriuria after KT on graft survival warrants further investigation