INTRODUCTION

Kidney transplantation is the most cost and clinically effective treatment for end-stage renal disease. While a successful renal transplant improves quality of life and reduces mortality risk for most patients when compared to dialysis, the altered anatomy of the urogenital tract and the use of immunosuppressive agents required to prevent acute rejection places patients at greater risk for post-transplant complications. Of these complications, bacterial infection is a major source of morbidity and mortality for renal transplant recipients. Urinary tract infections (UTI) remain a particularly common infectious complication in these patients. Bacteriuria can be divided into two categories: asymptomatic bacteriuria (ASB) and symptomatic UTI. ASB is defined as the outgrowth of bacteria with $>10^5$ CFU/mL from a properly collected urine sample, where the patient has no symptoms of infection. Historically, ASB was considered a harbinger of more serious infections or complications to the renal transplant patient and was universally treated. Recent evidence, however, indicates that treatment of ASB may not be necessary and is not associated with adverse graft outcomes. UTI, on the other hand, requires intervention and remains an ongoing challenge for infectious disease clinicians. Many bacteria species are responsible for UTI in renal transplant patients, and in recent years there has been a global rise in infection caused by bacteria with newly acquired antibacterial resistance genes. Many renal transplant patients who experience UTI will also have multiple recurring episodes, which likely has a distinct pathophysiological mechanism leading to chronic colonization of the urinary tract. In these cases, long-term management includes bacterial suppression, which aims to reduce rather than eliminate bacteria to levels below the threshold for symptomatic infection. This review will address the current understanding of UTI epidemiology, pathogenesis, and risk factors in the renal transplant community, and also focus on current prevention and treatment strategies for patients who face an environment of increasingly antibiotic-resistant bacteria.

KEYWORDS

bactiuria, methenamine, urinary tract infection
episodes, and receiving a kidney from a deceased donor.\textsuperscript{6} Compared to ASB, UTI may progress to sepsis, acute cellular rejection, impaired allograft function, allograft loss, and death, and are thus commonly treated with antibiotics depending on the susceptibility of the causative organism.\textsuperscript{7-10} While bacteria are the most common cause of UTI, fungal and mycobacterial infections can also occur.\textsuperscript{11-13} The most common bacterial causes of UTI are \textit{Escherichia coli}, \textit{Klebsiella pneumoniae}, \textit{Enterococcus} sp., \textit{Enterobacter}, \textit{Pseudomonas aeruginosa}, and \textit{Proteus mirabilis}.\textsuperscript{13,14} With the increasing worldwide prevalence of multidrug resistant (MDR) bacteria, such as extended-spectrum beta-lactamase (ESBL)–producing bacteria, UTI caused by these bacteria are increasingly challenging to treat.\textsuperscript{15,16} Likewise, studies have reported that anywhere from 4\% to 72\% (Table 1) of patients who develop one UTI will go on to develop recurrent UTI. The management of patients with recurrent UTI is challenging as the patients are repeatedly exposed to antibiotics, which can predispose them to infection by resistant organisms. In this review, we will summarize the current understanding of the epidemiology, treatment, prevention, and goals for future research for UTI in renal transplant recipients.

\section*{2 | CLINICAL DEFINITIONS}

Bacteria present in the urine with no local or systemic symptoms is defined as ASB (Table 2). A UTI, on the other hand, is defined as the presence of bacteriuria with signs and symptoms of infection, which range from mild irritative voiding to bacteremia or sepsis. UTI can affect the upper or lower urinary tract, and a UTI that leads to symptomatic infection of the bladder or kidney is referred to as cystitis and pyelonephritis, respectively.\textsuperscript{13} In renal transplant patients, infection of the transplanted kidney is referred to as allograft pyelonephritis (AGPN).\textsuperscript{17} Further distinctions within UTI can also be made. A UTI that occurs in the setting of a normal genitourinary tract with no prior instrumentation and/or only mild urinary symptoms is considered "uncomplicated," whereas infections that are diagnosed in genitourinary tracts with structural or functional abnormalities, such as indwelling urethral catheters, and/or are accompanied by more systemic symptoms is referred to as "complicated."\textsuperscript{18} A recurrent UTI is defined as \(\geq 3\) UTI episodes within 1 year or \(\geq 2\) UTI episodes in a 6-month period.

\section*{3 | PATHOGENESIS}

The pathogenesis of UTI typically involves a uropathogenic bacteria ascending to the bladder via the urethra. To accomplish this, bacteria often utilize adhesive molecules, such as \(P\) fimbriae in \textit{E. coli}, that help them adhere to the uroepithelium.\textsuperscript{19} Once in the bladder, bacteria can multiply and cause irritation to the bladder itself causing cystitis, or travel up the ureter and cause inflammation and AGPN.

Recurrent UTI can occur as either independent inoculations of the urinary tract or persistent infection of a foreign body (ie, stone, stent or drain) or organ or tissue (ie, prostatitis, pyelonephritis, or abscess). However, this model does not satisfactorily explain many recurrent UTI episodes in which the bacterial strains responsible for both the initial infection and the recurrence are genetically identical. It is hypothesized that recurrent UTI involves the formation of intracellular bacterial communities of bacteria. Uropathogenic \textit{E. coli} (UPEC) and \textit{K. pneumoniae}, for example, can enter the cytosol of superficial bladder cells and rapidly multiply, forming a biofilm-like assembly known as an intracellular bacterial community (IBC). The formation of IBCs can enhance the ability of these bacteria to establish themselves within the urinary tract and avoid urine flow, influx of inflammatory cells, and antibiotics. These intracellular bacteria can also enter a dormant state within the host epithelial cell actin, and become a quiescent intracellular reservoir in the intermediate and basal cells of the bladder that will periodically resurge and cause UTI.\textsuperscript{20,21}

\section*{4 | EPIDEMIOLOGY}

The prevalence of UTI in renal transplant patients tends to vary considerably between studies and locations, and has been reported to be as low as 7\% or as high as 80\% (see Table 1).\textsuperscript{22,23} Although differences in the definition of UTI, follow-up periods, geographical location, and prophylactic antimicrobial therapeutic regimen could all contribute to the variability in incidence of UTI between studies, UTI is quite common and affects many renal transplant recipients at some point in their lives. Although UTI can occur anytime following transplantation, they are most common during the first post-transplant year.\textsuperscript{24} Despite the frequency of bacteriuria, only about a third of patients who develop a UTI will experience recurrent UTI. In patients with bacteriuria, one study of 101 participants found that ASB, uncomplicated UTI, complicated UTI, and recurrent UTI occurred in 44, 32, 23, and 14\%, respectively.\textsuperscript{25}

\section*{5 | RISK FACTORS}

The risk of UTI in renal transplant patients includes factors that relate to the host, renal allograft, anatomical features of the recipient, and post-transplant hospital interventions. One common risk factor for UTI is the use of stents and catheters during and following the transplant procedure.\textsuperscript{26} In renal transplantation surgery, a shortened transplanted ureter is implanted into the recipient’s bladder directly and many surgeons choose to insert a stent to minimize the risk of major urological complications (eg, urine leak, obstruction) that can occur in the immediate post-transplant period. When surgeons choose not to use a stent, these patients can sometimes develop ureteric obstruction, which is also a risk factor for UTI.\textsuperscript{27} While some studies found no difference in the rate in patients with and without stents, the majority of studies have documented stents as being associated with higher rates of UTI.\textsuperscript{28-30} Stents are generally left in place for 4-6 weeks and are then removed. Early post-operative UTI are thought to be largely
## TABLE 1  Rate of UTI and recurrent UTI in kidney transplant studies

<table>
<thead>
<tr>
<th>Reference</th>
<th>UTI rate</th>
<th>Recurrent UTI rate</th>
<th>Study period</th>
<th>No. of patients</th>
<th>Patients with UTI</th>
<th>% Female</th>
<th>Age (year)</th>
<th>Follow-up (month)</th>
<th>Location</th>
</tr>
</thead>
<tbody>
<tr>
<td>54,a</td>
<td>-</td>
<td>36%</td>
<td>2001-2011</td>
<td>99</td>
<td>-</td>
<td>69%</td>
<td>53.3</td>
<td>54</td>
<td>Taiwan</td>
</tr>
<tr>
<td>42,a</td>
<td>-</td>
<td>72%</td>
<td>2010-2011</td>
<td>154</td>
<td>-</td>
<td>48%</td>
<td>51.3</td>
<td>12</td>
<td>Portugal</td>
</tr>
<tr>
<td>134,a</td>
<td>-</td>
<td>18%</td>
<td>1976-1994</td>
<td>307</td>
<td>-</td>
<td>87.5%</td>
<td>46</td>
<td>180</td>
<td>UK</td>
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<td>22</td>
<td>7%</td>
<td>-</td>
<td>1985-1999</td>
<td>954</td>
<td>68</td>
<td>24%</td>
<td>32.8</td>
<td>-</td>
<td>Turkey</td>
</tr>
<tr>
<td>46</td>
<td>13%&lt;sup&gt;a&lt;/sup&gt;</td>
<td>32%&lt;sup&gt;c&lt;/sup&gt;</td>
<td>1987-1999</td>
<td>1387</td>
<td>180</td>
<td>30%</td>
<td>44&lt;sup&gt;b&lt;/sup&gt;</td>
<td>&gt;12</td>
<td>France</td>
</tr>
<tr>
<td>34</td>
<td>15%</td>
<td>46%</td>
<td>2000-2010</td>
<td>344</td>
<td>50</td>
<td>72%</td>
<td>41.1</td>
<td>36</td>
<td>Korea</td>
</tr>
<tr>
<td>135,h</td>
<td>15%</td>
<td>15%</td>
<td>2003-2005</td>
<td>2174</td>
<td>150</td>
<td>33%&lt;sup&gt;b&lt;/sup&gt;</td>
<td>50&lt;sup&gt;b&lt;/sup&gt;</td>
<td>24</td>
<td>Spain</td>
</tr>
<tr>
<td>136</td>
<td>16%</td>
<td>-</td>
<td>2005-2007</td>
<td>158</td>
<td>25</td>
<td>31%</td>
<td>47</td>
<td>6</td>
<td>USA</td>
</tr>
<tr>
<td>39</td>
<td>17%&lt;sup&gt;a&lt;/sup&gt;</td>
<td>23%&lt;sup&gt;c&lt;/sup&gt;</td>
<td>1994-2004</td>
<td>1022</td>
<td>169</td>
<td>19%</td>
<td>34</td>
<td>&gt;6</td>
<td>India</td>
</tr>
<tr>
<td>52</td>
<td>18%</td>
<td>-</td>
<td>2002-2004</td>
<td>189</td>
<td>34</td>
<td>40%</td>
<td>49.7</td>
<td>36</td>
<td>Spain</td>
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<tr>
<td>17</td>
<td>20%</td>
<td>-</td>
<td>2005-2007</td>
<td>343</td>
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<td>44%</td>
<td>52</td>
<td>12</td>
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<td>9</td>
<td>21%</td>
<td>-</td>
<td>2005-2010</td>
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<td>247</td>
<td>39%</td>
<td>53</td>
<td>60</td>
<td>USA</td>
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<td>137</td>
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<td>-</td>
<td>2005-2013</td>
<td>9038</td>
<td>2100</td>
<td>39%</td>
<td>51</td>
<td>24</td>
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</tr>
<tr>
<td>75,h</td>
<td>24%</td>
<td>52%</td>
<td>2001-2004</td>
<td>127</td>
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<td>40%</td>
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<tr>
<td>48</td>
<td>28%</td>
<td>-</td>
<td>2012-2013</td>
<td>417</td>
<td>115</td>
<td>37%</td>
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<tr>
<td>138,f</td>
<td>31%</td>
<td>4%</td>
<td>2001-2007</td>
<td>598</td>
<td>185</td>
<td>35%</td>
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<td>32%</td>
<td>-</td>
<td>2000-2011</td>
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<td>19213</td>
<td>40%</td>
<td>-</td>
<td>54</td>
<td>USA</td>
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<td>66</td>
<td>33%</td>
<td>-</td>
<td>2009-2010</td>
<td>236</td>
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<td>39%</td>
<td>52</td>
<td>12</td>
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<tr>
<td>12</td>
<td>34%</td>
<td>-</td>
<td>2013-2014</td>
<td>120</td>
<td>41</td>
<td>38%</td>
<td>47.2</td>
<td>1</td>
<td>Poland</td>
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<td>25</td>
<td>34%</td>
<td>14%</td>
<td>2007-2009</td>
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<td>101</td>
<td>41%</td>
<td>56.7</td>
<td>10</td>
<td>USA</td>
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<td>36</td>
<td>36%</td>
<td>47.9</td>
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<td>2003-2007</td>
<td>176</td>
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<td>37</td>
<td>12</td>
<td>Mexico</td>
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<tr>
<td>140,h</td>
<td>37%</td>
<td>37%</td>
<td>1999-2001</td>
<td>52</td>
<td>19</td>
<td>42%</td>
<td>11-47</td>
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<td>Mexico</td>
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<tr>
<td>108</td>
<td>41%</td>
<td>36%</td>
<td>1999-2006</td>
<td>136</td>
<td>56</td>
<td>35%</td>
<td>31</td>
<td>38</td>
<td>Turkey</td>
</tr>
<tr>
<td>7</td>
<td>43%</td>
<td>64%&lt;sup&gt;c&lt;/sup&gt;</td>
<td>1996-2002</td>
<td>500</td>
<td>213</td>
<td>34%</td>
<td>44</td>
<td>42</td>
<td>USA</td>
</tr>
<tr>
<td>141</td>
<td>43%</td>
<td>-</td>
<td>1996-2000</td>
<td>28924</td>
<td>12508</td>
<td>40%</td>
<td>45.4</td>
<td>36</td>
<td>USA</td>
</tr>
<tr>
<td>34,h</td>
<td>45%</td>
<td>12%</td>
<td>2000-2001</td>
<td>163</td>
<td>73</td>
<td>40%</td>
<td>38</td>
<td>24</td>
<td>Brazil</td>
</tr>
<tr>
<td>142</td>
<td>55%</td>
<td>51%</td>
<td>2009</td>
<td>89</td>
<td>49</td>
<td>42%</td>
<td>48</td>
<td>12</td>
<td>Poland</td>
</tr>
<tr>
<td>51,d</td>
<td>61%</td>
<td>47%</td>
<td>1998-2008</td>
<td>122</td>
<td>74</td>
<td>38%</td>
<td>43.8</td>
<td>68</td>
<td>Greece</td>
</tr>
<tr>
<td>49</td>
<td>75%</td>
<td>-</td>
<td>2000-2005</td>
<td>172</td>
<td>133</td>
<td>32%</td>
<td>46.5</td>
<td>22</td>
<td>France</td>
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<tr>
<td>23</td>
<td>80%&lt;sup&gt;a&lt;/sup&gt;</td>
<td>-</td>
<td>1972-1991</td>
<td>576</td>
<td>464</td>
<td>45%</td>
<td>37.8</td>
<td>&gt;60</td>
<td>Germany</td>
</tr>
</tbody>
</table>

<sup>a</sup>Study looking at recurrent UTI only.
<sup>b</sup>For whole cohort, of which renal transplant patients were a subset.
<sup>c</sup>Recurrent UTI defined as having at least one episode of UTI.
<sup>d</sup>Dates for recurrent UTI represent patients with >3 UTI within study period, which may have been >1 year.
<sup>e</sup>Proportion patients who developed a UTI that went on to develop recurrent UTI.
<sup>f</sup>Recurrent infections were defined as UTI with two or more episodes during a follow-up period of 12 months.
<sup>g</sup>Study focused on AGPN only.
<sup>h</sup>Did not define criteria for recurrent UTI.
preventable and caused most frequently by contamination of a catheter at the time of insertion. The reason why stents and catheters increase the risk of UTI is thought to be because they can serve as reservoirs for bacteria. Stopping antibiotics without removal of the stent may predispose for UTI recurrence as well. Because of the UTI risk associated with stents and catheters, some clinicians choose to use perioperative antibiotic prophylaxis in order to reduce UTI risk in stented patients, and there is evidence that using TMP-SMX prophylaxis (discussed later) equalizes the risk of UTI in stented vs non-stented patients. The potential risk of UTI in stented patients has also led some groups to reserve stents only for select patients, such as those with existing damage or abnormalities in their native ureter, in order to decrease the likelihood of post-surgical complications.

Another anatomical consideration that predisposes renal transplant patients to a higher risk of infection, especially pyelonephritis, is the absence of a sphincter between the transplanted ureter and the native bladder, which increases the risk of vesicoureteral reflux or the retrograde passage of urine and potentially bacteria from the bladder into the upper urinary tract.

In addition to physical risk factors, the immunosuppressive drugs renal transplant patients must take to prevent graft rejection contribute varying degrees of risk for infection, including UTI. Adding thymoglobulin to a conventional immunosuppressive regimen, combination therapy with micro-emulsion form of cyclosporine A, prednisolone and azathioprine, and mycophenolate mofetil (MMF)-based treatment have been shown to impart a higher risk of UTI.

Other risk factors for UTI in renal transplant patients include female sex, older age, longer duration of catheter, receiving a transplant from a deceased donor, history of pre-operative UTI, and the occurrence of acute rejection. Some of these risk factors, such as female sex, are similar to those in the non-transplant population. The reason that female sex is thought to increase the risk of UTI is owing to the fact that women have shorter urethras and a urethral opening that is closer in proximity to the vagina and anus, which all provide a shorter pathway for bacterial migration compared to men. Risk factors for ESBL-producing bacteria (discussed later) include colonization with ESBL bacteria, delayed graft function, diabetes mellitus, previous antibiotic exposure, antibiotic prophylaxis, and recurrent UTI.

Predictive factors for recurrent UTI include nosocomial infection and MDR bacteria especially K. pneumoniae. The reason why infections by MDR organisms are associated with recurrent UTI remains unknown, but one possibility is that ESBL resistance co-localizes with other factors associated with an increase cell invasion and expression of fimbral adhesins. The ability for K. pneumoniae to form biofilm-like

### TABLE 2 Clinical definitions in renal transplant patients

<table>
<thead>
<tr>
<th>Asymptomatic Bacteriuria</th>
<th>&gt;10^5 bacterial colony-forming units per milliliter (CFU/mL) of urine</th>
<th>No local or systemic symptoms of UTI.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Uncomplicated UTI</td>
<td>&gt;10^5 bacterial colony-forming units per milliliter (CFU/mL) of urine</td>
<td>Dysuria, frequency, or urgency. (Functionally normal urinary tract)</td>
</tr>
<tr>
<td>Complicated UTI</td>
<td>&gt;10^5 bacterial colony-forming units per milliliter (CFU/mL) of urine</td>
<td>Fever, allograft pain, chills, malaise, or bacteremia with the same organism in urine. (Renal tract abnormalities)</td>
</tr>
<tr>
<td>Recurrent UTI</td>
<td>≥3 UTI in 1 year OR ≥2 UTI in 6 months</td>
<td></td>
</tr>
</tbody>
</table>

### TABLE 3 Associations among UTI, mortality, and graft loss

<table>
<thead>
<tr>
<th>References</th>
<th>Study dates</th>
<th>Sample size</th>
<th>Mortality (95% CI)</th>
<th>Graft loss (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>7</td>
<td>1996-2002</td>
<td>500</td>
<td>(OR) 3.5 (1.68-7.23)</td>
<td>NS</td>
</tr>
<tr>
<td>14</td>
<td>1996-2000</td>
<td>28,942</td>
<td>(AHR) 2.93 (2.22-3.85)</td>
<td>(AHR) 1.85 (1.29-2.64)</td>
</tr>
<tr>
<td>11</td>
<td>2000-2011</td>
<td>60,702</td>
<td>(AHR) 1.41 (1.25-1.56)</td>
<td>(AHR) 1.29 (1.16-1.43)</td>
</tr>
<tr>
<td>46</td>
<td>1987-1999</td>
<td>1,387</td>
<td>-</td>
<td>(RR) 3.6 (1.4-9.2)</td>
</tr>
<tr>
<td>50</td>
<td>2010</td>
<td>105</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>25</td>
<td>2007-2009</td>
<td>301</td>
<td>-</td>
<td>NS</td>
</tr>
<tr>
<td>49</td>
<td>2000-2005</td>
<td>172</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>12</td>
<td>2013-2014</td>
<td>120</td>
<td>NS</td>
<td>NS</td>
</tr>
</tbody>
</table>

UTI alone, risk during first year (UTI alone, risk after 1 year: AHR 1.16 [95% CI 1.11-1.21]).

Occurrence of AGPN during the first 3 months post-transplant.

Statistics reflect 1-year graft function and survival.
intracellular bacterial communities within epithelial bladder cells is determined by its fimbrial adhesins, called a type 1 pilus, and greater expression of this protein enhances the ability of *K. pneumoniae* to colonize the urinary tract and form IBCs and biofilms.21

6 | IMPACT OF UTI ON PATIENT OUTCOMES

When renal transplant patients contract a UTI, the feared outcome is impaired allograft function, graft loss, and a higher risk of mortality, but the significance of the link between UTI and these outcomes is not perfectly clear. Table 3 summarizes some key research addressing the association among UTI, mortality, and graft loss. A few heavily cited studies published in the early 2000s found that UTI was associated with an increase in mortality and increased the risk of allograft loss.7,8 In support of these findings, a more recent study of Medicare-insured renal transplant recipients between 2000 and 2011 found that UTI within the first year post-transplant was associated with a 41% increase in mortality risk and a 29% increase in risk of graft loss.11 Other analyses of the long-term impact of UTI have found more nuanced relationships, such as one study that found significantly detrimental outcomes for graft survival only when a UTI was contracted within the first 3 months post-transplant46 or that AGPN is associated with a decline in renal graft function as measured by creatinine clearance or GFR12,43,47,48 but does not necessarily affect allograft loss.49 Along with studies investigating the survival and function of the transplanted kidney, studies have found that UTI can cause other negative health outcomes, such as increasing the length of stay in the hospital post-transplant and the risk of reoperation.12 Evidence also suggests that UTI within the first 3 months post-transplant that go untreated can increase risk of acute cellular rejection.7

In the literature, there are also studies that argue UTI has no impact on graft function or survival.50 In a study of 122 patients the authors found that long-term renal graft function, as measured by serum creatinine, was no different 5 years post-transplant between patients who had experienced zero, one, or multiple episodes of UTI.51 In a study of 189 renal transplant patients the authors similarly concluded that in their 36 months follow-up, graft function did not differ significantly between recipients with or without AGPN.52

### TABLE 4 Associations between UTI and kidney function

<table>
<thead>
<tr>
<th>Reference</th>
<th>Date range of study</th>
<th>No. of participants</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Impact</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>49</td>
<td>2000-2005</td>
<td>172</td>
<td>Significantly lower in patients with AGPN compared to uncomplicated UTI and no UTI up to 4 years post-transplant</td>
</tr>
<tr>
<td>43</td>
<td>2000-2010</td>
<td>344</td>
<td>eGFR decreased significantly faster in UTI group compared to non-UTI group</td>
</tr>
<tr>
<td>12</td>
<td>2013-2014</td>
<td>120</td>
<td>GFR was significantly decreased at 14 days in bacterial infection group (82% of which was UTI, but also included other infection sites)</td>
</tr>
<tr>
<td>47</td>
<td>2001-2011</td>
<td>265</td>
<td>Early-onset graft pyelonephritis resulted in a &gt;30% reduction in eGFR over 2 years compared to patients without early-onset graft pyelonephritis</td>
</tr>
<tr>
<td>48</td>
<td>2012-2013</td>
<td>417</td>
<td>Mean GFR was significantly lower in patients with a UTI at 3, 6, 9, and 12 months post-operatively compared to patients without UTI</td>
</tr>
<tr>
<td>143</td>
<td>2007-2013</td>
<td>141</td>
<td>UTI associated with significantly lower eGFR 1 year after transplantation</td>
</tr>
<tr>
<td>No impact</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>25</td>
<td>2007-2009</td>
<td>301</td>
<td>No difference in eGFR or serum creatinine between UTI and no UTI group at 1-year follow-up, however, iGFR was significantly lower in UTI group</td>
</tr>
<tr>
<td>50</td>
<td>2010</td>
<td>105</td>
<td>No difference in GFR was observed between UTI and no UTI groups 1-year follow-up</td>
</tr>
<tr>
<td>51</td>
<td>1998-2008</td>
<td>122</td>
<td>No difference in serum creatinine between UTI and no UTI group up to 5 years follow-up</td>
</tr>
<tr>
<td>52</td>
<td>2002-2004</td>
<td>189</td>
<td>No difference in serum creatinine between UTI and no UTI group up to 36 months follow-up</td>
</tr>
</tbody>
</table>
who received renal transplantation at the Mayo Clinic between June 2007 and June 2009 found that when kidney function was measured by eGFR and creatinine, there was no significant difference in allograft function between kidney recipients with or without UTI. However, when the authors compared kidney function by iohalamate glomerular filtration rate (iGFR), it was significantly lower in patients who had developed at least one UTI after transplantation.25 Table 4 summarizes literature associating between UTI and renal function.

In addition to mortality and graft function, UTI also increase the risk of other complications. One complication is bacteremia secondary to bacteria migrating from the urinary tract into the blood stream.9,53 Risk factors for bacteremia after UTI include immunosuppression with tacrolimus and a baseline serum creatinine level >1.3 mg/dL before first UTI.54 Upper UTI could also potentially progress to a rare condition called emphysematous AGPN.55 Emphysematous AGPN is a life-threatening complication that can lead to graft loss and is characterized by necrotizing infection of the renal parenchyma and perirenal tissue, which results in the presence of gas within the renal parenchyma, collecting system, or perinephric tissue.56 Although there is debate as to what extent UTI can influence morbidity and mortality in renal transplant patients, most studies have demonstrated an impact on patient and graft outcomes.

7  |  MICROBIOLOGY

The most common bacterial species that cause UTI in renal transplant patients are E. coli, Enterococcus sp., and Klebsiella sp.57 While E. coli is a common cause of UTI in both renal transplant recipients and non-recipient patients, Klebsiella tends to colonize renal transplant patients more frequently.58 The relative prevalence of one bacterial species vs another tends to change depending on the time of UTI post-transplant.59 For example, one center found that Enterococcus was the most common cause of UTI in patients in their first month post-transplant, while E. coli was the most common in patients during their second month post-transplant. While bacteria are the predominant cause of UTI, a smaller percentage of cases can be caused by fungal organisms such as Candida spp. and clinicians must be aware of this possibility.

8  |  PREVENTION AND PROPHYLAXIS

UTI is the primary driver of antibiotic administration to renal transplant patients. In an effort to reduce UTI, antibiotic prophylaxis during the perioperative period is widely accepted as the standard of care. However, there remains to be a consensus within the transplant community regarding the ideal preventive strategy. Based on several clinical trials in the 1980s and 90s, the current mainstay of UTI prophylaxis is trimethoprim-sulfamethoxazole (TMP-SMX), which is also used for 6-12 months after transplantation for the prevention of Pneumocystis jirovecii pneumonia (PCP).50-53 Patients who receive PCP prophylaxis with TMP-SMX are less likely to develop UTI compared to those who receive other prophylaxis, such as pentamidine or oral dapsone, and TMP-SMX has also been shown to reduce the occurrence of bacteruria and sepsis with bacteremia.17,64 The prophylactic effect of TMP-SMZ is most pronounced during the first year after transplantation but is attenuated over time, becoming less significant by the second year after transplantation.57 Some studies have also shown that using ciprofloxacin in addition to TMP-SMX further reduces the incidence of UTI by 12%-20% compared to TMP-SMX alone.55,66 Ciprofloxacin used as prophylaxis at the time of urinary catheter removal has also been shown to reduce the incidence of UTI by 40%.67 Although several trials have compared the impact of prophylaxis with placebo or no intervention on post-surgical complications in renal transplant patients, meta-analyses of these trials found no difference in all-cause mortality, rejection, or major adverse events between treatments groups.64 Despite this finding, prophylaxis with TMP-SMX is still recommended by guidelines. Patients who are intolerant or allergic to TMP-SMX typically receive atovaquone, dapsone, or aerosolized pentamidine, which do not possess antibacterial properties and therefore would not prevent the development of UTI.5,68 When agents other than TMP-SMX are utilized, current guidelines recommend the use of an antibiotic for at least as long as the stent is in place. A study in 2011 found that prophylaxis with the fluoroquinolone ofloxacin for the first month plus TMP-SMX for 3 months reduced the 1-year incidence of UTI and AGPN in renal transplant patients compared to TMP-SMX prophylaxis alone, and treatment with ofloxacin + TMP-SMX actually decreased need for subsequent therapeutic antibiotics.69 However, use of ofloxacin prophylaxis led to increasing fluoroquinolone resistance in Pseudomonas aeruginosa and is thus not recommended in guidelines. Cephalexin has been shown to be useful as prophylaxis in one older study, and is the preferred prophylactic by some clinicians for patients who do not tolerate TMP-SMX.64 There is, however, limited information regarding cefepime compared to TMP-SMX. In the study using cefepime as UTI prophylaxis in kidney transplant patients, the authors gave cefepime 250 mg 1/day to 35 patients, and saw that at the end of 4 months 1/35 patients developed bacteriuria.70 Clinicians should take care, however, as the use of cephalosporins in prophylaxis undoubtedly increases bacterial resistance to other third-generation cephalosporins.71 In addition to post-surgical prophylaxis, some clinicians also choose to use perioperative prophylaxis at the time of renal transplant. Although there is no consensus on the use of perioperative prophylaxis in the transplant population, some studies with small sample sizes in renal transplant patients suggest that perioperative ceftriaxone can effectively prevent UTI and surgical site infections.72,73 Meta-analysis of ceftriaxone prophylaxis in the general patient population has also supported its efficacy in preventing UTI, although resistance is still always a concern.74 Beyond prophylaxis with TMP-SMX there is little consensus about the appropriate UTI prophylactic strategy. When deciding on prophylactic therapy for patients unable to take TMP-SMX, clinicians must ultimately depend on the patient’s current and past microbiology data and on local resistance patterns at the transplant center.
Besides pharmacological therapy, risk modification is also an important step in preventing UTI. A recent study provides strong evidence that early removal of stents can reduce risk of UTI. In the study, the authors randomly assigned 103 renal transplant recipients to either have early ureteral stent removal at 1 week or routine ureteral stent removal at 4 weeks, and then patients were followed for 3 months for UTI-related complications. The study found that the early stent removal group has a significantly smaller incidence of UTI (5.8% in the early stent removal group compared with 29% in the routine stent removal group). The justification for leaving stents in place longer is often to reduce ureteral mechanical complications; however, in the study the authors did not note any mechanical complications in either group, which suggests that stent placement for 1 week may be optimal in preventing both mechanical complications as well as minimizing UTI risk. In addition to early stent removal, other risk-modifying behaviors that have been studied include avoiding azathioprine, sirolimus, or MMF-based immunosuppression, and avoiding the use of thymoglobulin for induction therapy.

The major concern with using antibiotics prophylactically is that it will contribute to a rise in bacterial resistance. TMP-SMX administration has been shown to increase the percentage of bacteria-isolated resistant to amoxicillin and TMP-SMX. Given the risk of resistance, some have advocated for reduced use of antibiotics with a focus in selected high-risk patients. Ultimately an analysis of the local incidence of UTI is key to determining what level of prophylaxis should be used and is setting specific.

9 | DIAGNOSIS OF URINARY TRACT INFECTIONS

Patients with cystitis will typically have symptoms that include dysuria, frequency, or urgency. In the case of pyelonephritis, patients may also have allograft pain, although because the transplanted kidney is not innervated, pain may not always be present. Patients with symptoms of a UTI should then have a urine analysis performed. Indicators of infection include presence of leukocyte esterase, nitrites, and blood. If urine microscopy is performed, pyuria (at least 10 white blood cells per high-power field of unspun urine) and presence of bacteria or yeast may be noted. While pyuria does not necessarily confirm a UTI, the absence of pyuria should lead the clinician to reconsider the differential of UTI. Diagnosis of UTI is established by a quantitative count of bacteria (≥10^5) in an appropriately collected urine specimen in the presence of signs or symptoms of urinary infection.

It should be noted that not all organisms found in urine cultures are pathogens. For example, *Staphylococcus epidermidis* (except in the presence of ureteral stents), *Lactobacillus*, and *Gardnerella vaginalis* are uncommonly responsible for UTI. Urine cultures containing multiple organisms indicate that the sample may be contaminated or collected without proper sterile technique. In other circumstances, true pathogens may not grow well on routine culture media, such as the unusual pathogens *Corynebacterium urealyticum* or *M. tuberculosis*, and special culture media may be required. *C. urealyticum* is a slow-growing organism that requires selective media for isolation. *C. urealyticum* should be suspected if renal transplant patients present with any of the following: chronic UTI symptoms with negative conventional urine cultures, alkaline urine (pH >7), pyuria or microscopic hematuria with no other explanation, presence of struvite crystals, obstructive uropathy, and encrusting cystitis or pyelitis.

In addition to laboratory testing, clinicians can also use imaging with renal ultrasound or non-contrast CT scan to assess for complications such as obstruction and abscess, and this is especially helpful to assess patients who do not fully respond to initial therapy or those with signs of severe infection.

10 | ASYMPTOMATIC BACTERIURIAS

Asymptomatic bacteriuria is a common event after renal transplantation, with rates up to 51%. Historically bacteriuria was considered a risk factor for progression to UTI and pyelonephritis which could then lead to graft dysfunction and early failure. As a result of these concerns, many clinicians treat patients with ASB with unclear or incorrect knowledge about the impact of this treatment on patient outcomes. While there is some evidence that suggests ASB can have a negative impact on renal transplant patients, more contemporary data suggest that ASB is not equivalent to UTI and should not be treated. Older studies that show negative outcomes of ASB include one study that suggested ASB is an independent risk factor for bacteremia. A few other studies argue that recurrent ASB increases the risk of AGPN and organ rejection, but does not impair long-term graft function. However, a recent landmark clinical trial by Origuen et al. has provided strong evidence that clinicians should not treat ASB. In the study, the authors randomized 112 patients into two groups, one that would receive systematic antimicrobial therapy for all episodes of ASB occurring between 2 and 24 months after transplantation, and a control group that received no therapy. Both groups received similar systematic screening for ASB. Strikingly, the authors found that their primary outcome, the occurrence of acute pyelonephritis at 24 months follow-up, was no different between groups. What’s more, the authors also found no difference in rates of lower UTI, acute rejection, *Clostridium difficile* infection, colonization or infection by multidrug-resistant bacteria, graft function, or all-cause mortality between groups. Although the study by Origuen et al. was not the first to come to their conclusion, they improved upon a previous study by following patients in the critical early post-operative period. In addition to the study by Origuen et al., two other retrospective studies have similarly found no benefit to treating ASB, with one study finding that treatment even increased the risk of symptomatic UTI and the total number of hospitalization days at 6 months post-ASB. Although the best randomized control trial thus far by Origuen et al. did have a limited sample size, evidence suggests that clinicians should avoid treating ASB, which can overexpose renal transplant recipients to antibiotics and contribute to antibacterial resistance.
Owing to their concern of ASB becoming symptomatic UTI, some clinicians also actively screen renal transplants in the post-operative period. However, there is not conclusive evidence that suggests screening for ASB improves outcomes. In 2005, the Infectious Disease Society of America published in their guidelines “No recommendation can be made for screening for or treatment of ASB in renal transplant or other solid organ transplant recipients.” Data suggest that ASB in fact often spontaneously clears without antibiotics and use of antibiotics drive resistance and other complications (ie, C. difficile colitis). Thus, given the available information, clinicians should adopt a more conservative approach in the management of ASB with observation without antibiotics in most cases.

With regards to much less prevalent fungal pathogens, while more serious and symptomatic fungal UTI increases the risk of graft loss and requires treatment, there has not been sufficient evidence to support the treatment of asymptomatic candiduria in the renal transplant population. There tends to be no differences in outcomes between patients that are treated for asymptomatic candiduria and those who are not.

11 | TREATMENT OF URINARY TRACT INFECTIONS

Patients with symptoms of a UTI or pyelonephritis and a positive urinalysis (urine dipstick with leukocyte esterase, nitrite, and blood, and urine microscopy showing pyuria) and a positive urine culture (≥10^5 colony-forming units [CFU]/mL) should have antibiotics initiated empirically (see Table 2). Factors to take into account when determining empiric coverage includes the local epidemiology of resistance at your center, susceptibilities in prior UTI in the patient, severity of illness (ie, need for IV therapy), recent antibiotics given, and allergies. A urinalysis and urine cultures should be performed before the administration of antibiotics to determine antibiotic susceptibilities of the microorganism. Once susceptibility results are available, the therapy should be changed to reflect the resistance pattern of the isolated organisms while also maintaining the narrowest spectrum to avoid future resistance. For uncomplicated UTI, empiric antibiotic therapy is generally given orally, while empiric therapy for complicated UTI is often given intravenously to cover gram-negative and gram-positive bacteria. While many may consider UTI in transplant patients complicated in most cases, patients without systemic evidence of involvement (ie, renal dysfunction, graft tenderness, and fever) and without abnormalities of the collecting system (ie, hydronephrosis or stones) can likely be treated as an outpatient with oral therapy. Historically, fluoroquinolones, particularly ciprofloxacin, were commonly used for empiric therapy. However, most centers have relatively high rates of fluoroquinolone resistance in common UTI bacteria and in 2016 the FDA also stated that fluoroquinolones should only be used for uncomplicated UTI treatment for patients who do not have alternative treatment options, as a result of the serious side effects of the medication. This has led most clinicians to recommend other initial therapies, including cephalexin or nitrofurantoin (see below, requires adequate GFR). Clinicians must also consider the potential for multidrug-resistant organisms (MDROs), which may require more aggressive treatment with carbapenems or other antibiotics available for resistant strains.

Faced with increasing antibiotic resistance to commonly used UTI antibiotics like ciprofloxacin, antibiotic treatments for UTI caused by ESBL-producing bacteria include piperacillin-tazobactam and imipenem. Carbapenems are still the preferred drug of choice for infections owing to ESBL-producing bacteria as they are generally resistant to ESBL-mediated hydrolysis. Carbapenems and fosfomycin are also emerging antibiotic choices for UTI caused by ESBL organisms, as they have been shown to have a high level of broad-spectrum antimicrobial activity against ESBL bacteria. Carbapenem resistance has also begun to emerge in Enterobacteriaceae, creating new treatment challenges for UTI caused by carbapenem-resistant Enterobacteriaceae (CRE). Management of CRE UTI is difficult as it requires the use of nephrotoxic antibiotics (eg, aminoglycosides, polymyxins) that can cause permanent damage to the transplanted graft. Aminoglycosides and polymyxins also have increased risk of nephrotoxicity when used in patients also taking calcineurin inhibitor-based immunosuppression, which is common in transplant patients.

While many drugs can be utilized for UTI, some do not concentrate well in various components of the urinary tract to be safely used in select settings. Moxifloxacin does not penetrate well into the urine and therefore is not recommended for treatment of UTI or pyelonephritis. Two other drugs, nitrofurantoin and fosfomycin, should not be used in patients with reduced GFR. Nitrofurantoin is not recommended for patients with creatinine clearances <20 mL/min, as they excrete little or no drug in the urine. Fosfomycin is generally restricted for patients with a creatinine clearance above 45 mL/min. These agents are generally not utilized in cases of pyelonephritis owing to limited parenchymal concentration.

12 | MANAGEMENT STRATEGIES FOR SUBJECTS WITH RECURRENT UTI

Patients with recurrent UTI are both a concern and a challenge for clinicians. Frequent UTI may be associated with worse outcomes. Furthermore, recurrent UTI result in frequent calls and visits to the clinician to manage the UTI. Over time, patients with recurrent UTI develop increasing resistance in infecting bacteria reducing the options for management and may eventually lead to requirement of intravenous therapies. Given the challenges and impact of recurrent UTI, aggressive approach to evaluate for resolvable sources of recurrence and suppressive therapies should be considered.

The general evaluation for recurrent UTI involves first investigating whether there are any correctable anatomical or functional abnormalities in the urinary tract that could be contributing to increased infection risk. To accomplish this, clinicians can use radiographs, ultrasound, or computerized tomography of the transplanted and native kidneys, ureters, and bladder. Potential complications that could
be contributing to recurrent UTI include urinary tract obstruction, strictures, stenosis, renal calculi, and complex cysts. Urinary tract obstruction, strictures, stenosis, renal calculi, and complex cysts. Further investigation of complications may also require other imaging methods, such as CT-PET for patients with suspected polycystic kidney disease, cystoscopy for patients with potential abnormalities of the urethra and bladder, and voiding cystourethrography for patients with suspected vesicoureteral reflux. Bladder dysfunction and outflow tract obstruction may also be diagnosed using urodynamic studies.106

13 | PREVENTION OF RECURRENT UTI

Prevention of recurrent UTI in transplant patients has not been well investigated, and current therapies tend to have some overlap with strategies aimed to prevent recurrent UTI in the non-transplant population. Prevention involves behavior education, antimicrobial prophylaxis, and a variety of other interventions.

In the clinic, behavioral education is the first tool that clinicians can universally use to help prevent UTI in both renal transplant and non-transplant patients. Some of the most important behavioral factors that contribute to recurrent UTI are sexual intercourse, a new sex partner, and the use of spermicides. Post-coital voiding and liberal fluid intake to increase the frequency of micturition may also be helpful, and while these behaviors have not been supported in controlled studies, they are unlikely to be harmful.107

Another strategy to prevent recurrent UTI is through the use of antibiotic suppression, although there are few studies on antibiotic suppression in renal transplant patients. One small study in renal transplant patients tested nitrofurantoin in 15 patients with recurrent UTI, but the authors deemed it ineffective as 12 of the 15 patients continued to develop UTI.108 In contrast, with non-transplant patients, there is good evidence that antibiotic prophylaxis is useful in prevention of recurrent UTI. A meta-analysis concluded that antibiotic treatment with trimethoprim/sulfamethoxazole, nitrofurantoin, cephalexin, or norfloxacin/cinocinax reduced the number of clinical and microbiological recurrences of UTI compared to placebo in pre- and post-menopausal women with previous recurrent UTI.109 The study noted that while there is a preventative effect, once antibiotics are suspended, UTI recur in patients to the same level as those of the placebo group. In terms of drawbacks, as with all antibiotic therapy, side effects can be cumbersome for patients, and long-term antibiotic use will only lead to greater bacterial resistance.

In addition to suppressive antibiotics, clinicians can also use suppressive therapy with antimicrobial agents like methenamine hippurate, which has been demonstrated to reduce the frequency of UTI in non-transplant patients. Methenamine was first introduced as a urinary antiseptic in 1899,110 and it is an organic compound that, when taken orally, travels to the bladder where it decomposes in the acidic environment to form formaldehyde and ammonia. Formaldehyde inactivates microorganisms by non-specifically alkylating the amino and sulfhydryl groups of proteins and ring nitrogen atoms of purine bases. Owing to this mechanism, bacteria may be less capable of developing resistance to methenamine and it thus offers an appealing alternative to conventional targeted antibiotics. A recent meta-analysis concluded that methenamine hippurate may be effective in preventing UTI in patients without renal tract abnormalities, particularly when used for short-term prophylaxis. Although the authors mention that methenamine does not appear to be effective for long-term prophylaxis in studies with patients who have neuropathic bladder,111 well-controlled randomized controlled trials are still necessary to clarify whether longer-term methenamine prophylaxis is useful in preventing recurrent UTI in renal transplant patients.

Considering non-antimicrobial therapy, one study showed that cranberry juice and L-methionine successfully reduce the incidence of and symptoms of recurrent UTI in renal transplant patients.112 A meta-analysis in non-transplant women also has provided evidence that cranberry juice can prevent recurrent UTI in this group.113 Cranberry juice has been known as a folk remedy to prevent UTI and has been shown to reduce the adherence of E. coli to uroepithelial cells by preventing adhesion of the bacterial P fimbriae to the uroepithelium.114 L-methionine acidifies the urine and is thought to also decrease bacterial adherence to uroepithelial cells. There is limited risk with these two interventions and many clinicians utilize these in patients with recurrent therapy as an adjunct to more active therapies.

Other treatment strategies to reduce UTI have been investigated in non-transplant patients, but may offer some insight into future strategies for renal transplant recipients. A meta-analysis of post-menopausal women concluded that based on two studies comparing vaginal estrogens to placebo, vaginal estrogens reduced the number of UTI.115 Combination of hyaluronic acid (HA) and chondroitin sulfate, which is thought to help promote a healthy mucopolysaccharide film coating on the urothelium, has also been used to reduce the incidence of recurrent cystitis in post-menopausal women.116,117 In liver transplant patients, evidence suggests that the use of probiotics reduces the incidence of bacterial infections including UTI after transplantation.118 Finally, one study found that a low vaginal pH produced by vaginal Lactobacillus colonization may drop recurrences of UTI in non-transplant women.119 While these treatments may be useful for non-transplant patients, further study is needed to investigate whether the results apply to the renal transplant population.

Looking into the future, some emerging strategies to prevent UTI in non-transplant patients, which could potentially be important for transplant recipients, include compounds aimed at preventing urothelial bacterial adhesion. With greater knowledge of the intracellular assembly process of bacterial pili, researchers are currently developing molecules termed pilicides to block this process and prevent bacteria adhering to urothelial cells and creating subsequent reservoirs.120 Although these molecules have yet to be tested in animal models, other molecules that block bacterial adhesins, called mannosides, are also in development, and have also been shown to be effective at preventing UTI in murine models.121 Other potential therapies include the development of bacterial vaccines, which have targeted a variety of bacterial proteins including adhesins, virulence factors, and iron receptors.122 Although great strides have been made in developing new strategies to treat UTI, the greatest concern is the impact
these strategies will have on the endogenous microbiome. Systemic administration of mannosides, pilicides, and antibacterial vaccines have the potential to target beneficial bacterial communities within the body. The effectiveness of these strategies is thus still unclear and trials are currently underway.

14 | BACTERIAL RESISTANCE

The rise in bacterial resistance worldwide is one of the most significant challenges that the field of transplant medicine currently faces. More detailed reviews of mechanisms and management of multidrug-resistant gram-negative bacteria can be found elsewhere. ESBL-producing gram-negative bacteria and CRE, including carbapenem-resistant K. pneumoniae, are increasingly causes of UTI in renal transplant recipients. A recent meta-analysis of the literature found that the incidence of UTI caused by ESBL-producing Enterobacteriaceae in renal transplant patients is 10%. Fortunately, outcomes for UTI caused by these resistant bacteria are generally excellent, although their management is far more complicated. Oral therapy that remain active against many of these resistant bacteria includes nitrofurantoin, fosfomycin, and minocycline, while IV options include carbapenems for ESBL organisms and amikacin and colistin for CRE. Of the multidrug-resistant bacterial causes of UTI, ESBL bacteria are more common than CRE infections, and patients generally clear infections successfully when treated with a carbapenem. Case studies have shown that some CRE strains can have successful therapeutic clearance when being treated with colistin, doxycycline, or high-dose meropenem, though. However, one of the most recent and concerning evolutions of CRE organisms are bacteria containing the New Delhi Metallo-beta-lactamase-1 (NDM-1). Several case studies patients with UTI caused by NDM-1 have been reported in the literature, some with successful treatment outcomes and others with failure leading to graftectomy. Risk factors for ESBL UTI include diabetes mellitus, previous antibiotic prophylaxis or therapy, previous UTI, recurrent infection, and patients with delayed graft function after transplant. Risk factors for CRE UTI have not been studied well, but certainly include use of carbapenem antibiotics. Pyelonephritis caused by carbapenem-resistant K. pneumoniae are also associated with greater odds of failure to clear bacteria 72 hours after treatment, occur earlier after transplantation than those owing to susceptible K. pneumoniae, and are associated with a urinary catheter at diagnosis, a 24-hour stay in the ICU either before or after development of the UTI, and a longer length of stay in the hospital prior to the UTI.

15 | HEALTHCARE COST OF UTI

UTI are a major driver of cost in renal transplant patients and prevention strategies may reduce overall costs. In a study of 60,702 renal transplant recipients in the United States between 2000 and 2011, infections from UTI increased first year costs by $17,691, and the increased costs persisted for 2-3 years post-transplant. In another study of 90 patients who underwent renal transplantation in Thailand, UTI increased the overall cost of treatment per patient by $5,131. Because UTI tends to increase the length of hospital stay for renal transplant patients, it also logically increases the cost of care.

16 | CONCLUSIONS

UTI remain one of the most frequent complications in renal transplantation that have negative consequences to both the patient and the graft. Current data suggest that ASB is not generally associated with development of symptomatic disease or graft dysfunction and therefore should not be screened for or treated. Treatment of UTI should focus on the narrowest spectrum antibiotic to minimize the emergence of resistance. Management of UTI caused by MDROs is more complicated and required tailored therapy. Recurrent UTI are a major driver for resistance emergence and should be evaluated for reversible causes and managed with non-antibiotic-suppressive strategies when possible. Given the current challenges and impact of UTI, future studies should focus on optimal prevention and treatment strategies to minimize the impact of these common infections.

AUTHOR CONTRIBUTIONS

Both Mr. Hollyer and Dr. Ison contributed equally to the review of the existing literature, drafting the article, and approval of the final document.

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REFERENCES


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