

Original Article | **Clinical Significance of Bacteriuria in Patients with Orthotopic Sigmoid Neobladder after Radical Cystectomy**

**E. Elsotohi**

*Department of Urology Al-Azhar University, Cairo, Egypt*

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**ABSTRACT**

**Objectives:** To evaluate the incidence and clinical significance of bacteriuria in patients who underwent sigmoid neobladder substitution after radical cystectomy.

**Patients and Methods:** The study included 149 patients with invasive bladder carcinoma who underwent radical cystectomy and orthotopic sigmoid bladder substitution. Diagnosis of bacteriuria was made by freshly collected midstream urine culture at 3, 6 and 12 months post-operatively. Positive urinary culture was defined as >100 000 colony forming units (CFU)/ml. The data collected were evaluated in correlation to the clinical status of the patients.

**Results:** Overall 466 urine samples from 149 patients were cultured during the follow-up period. Out of these 149 patients, 18 were lost to follow-up and 11 patients developed new stone formation in the neobladder with an incidence of bacteriuria of 91%. These 29 patients were excluded from the study. Among the remaining 120 patients, positive urine culture with significant growth of uropathogens was seen in 64%, 47% and 33% at 3, 6 and 12 months, respectively. Two thirds of patients with positive urine cultures were asymptomatic. The commonest uropathogen encountered was *E Coli* (72%) followed by *Klebsiella* (12%).

**Conclusion:** Sigmoid neobladder substitution is associated with a high incidence of bacteriuria. Despite, the spontaneous clearance of bacteriuria over time without antimicrobial manipulation, antimicrobial therapy was needed in some patients, particularly those with a large post-void residual (PVR) urine volume, persistent urosepsis and stone formation in the neobladder.

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**Key Words :** Urinary tract infection, bacteriuria, radical cystectomy, neobladder

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**Corresponding Author:** Dr.Ebrahim Elsotohi, Department of Urology, Al-Hussein University Hospital, Cairo, Egypt, Email: ebrahim\_elsotohi@yahoo.com

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**Article Info:** Date received : 29/3/2009

Date accepted (after revision): 22/12/2009

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**INTRODUCTION**

For the past few decades radical cystectomy has been the gold standard for the treatment of muscle-invasive bladder carcinoma<sup>1,2</sup> while orthotopic bladder substitution is considered by many authors as the most desirable and socially most convenient form of urinary diversion<sup>3,4</sup>. Although incorporation of bowel into the urinary tract may be associated with an increased frequency of bacteriuria, its mechanism is not clear<sup>5</sup>. Therefore, the study of bacteriuria in patients with orthotopic urinary reservoirs is important because urinary tract infection (UTI) is a frequent cause of

fever and deterioration of renal function<sup>6</sup>. The present study was designed to evaluate the frequency of bacteriuria and its sequelae in patients with a sigmoid neobladder.

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**PATIENTS AND METHODS**

Between April 2002 and October 2007, 149 patients with invasive bladder carcinoma underwent radical cystectomy and orthotopic sigmoid neobladder substitution in the

Urology Department of Al-Hussein Teaching Hospital, Al-Azhar University, Cairo, Egypt. The study group included 125 male and 24 female patients with a mean age of  $52 \pm 16.4$  (range 30 – 78) years.

Patients with local tumor recurrence, upper-tract obstruction, chronic retention, renal calculi and ureteral reflux were excluded from the study. Urine analysis, midstream urine culture and pelviabdominal ultrasound were performed to evaluate the incidence of UTI and Post Voiding Residual (PVR). Bladder emptying was considered complete when the mean post-void residual urine (PVR) was  $<20\%$  of the voided volume in repeated measurements by ultrasonography<sup>7</sup>.

In male patients urine samples were taken by clean midstream urine sampling, while in female patients the urine samples were collected via urethral catheterization under aseptic conditions. The urine samples were cultured in aerobic and anaerobic media to identify uropathogenic organisms. Bacteriuria was defined as the presence of at least 100 000 “Colony Forming Units” (CFU) of bacteria/ml urine. Follow-up was carried out at 3, 6 and 12 months.

## RESULTS

Overall 466 urine samples from 149 patients were cultured. Of these, 18 patients did not complete the follow-up and 11 developed new stone formation in the sigmoid neobladder with an incidence of significant bacteriuria in 91%. These 29 patients were excluded from the study. Of the remaining 120 patients, 64% showed a positive culture with significant growth of uropathogens 3 months post-operatively. There was a steady decline in the incidence of positive cultures to 47% and 33% at 6 and 12 months respectively ( $p < 0.05$ ) (Fig.1).

Due to a high PVR clean intermittent self-catheterization (CIC) was required in 20 patients; all of them had positive cultures during the follow-up period with a gradual decrease

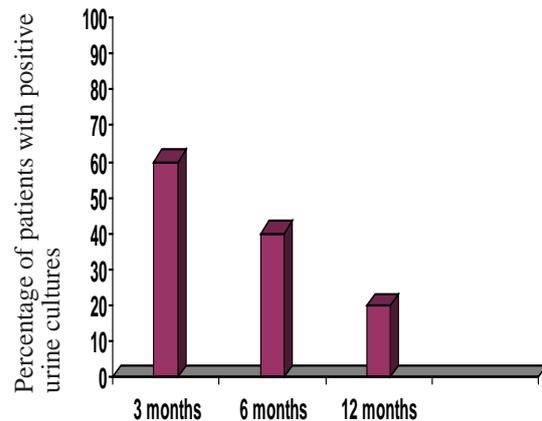


Fig. 1: Decreasing incidence of bacteriuria during follow-up

in CFU/ml urine. There was no significant difference between patients with and without CIC regarding the degree of gradual decline of bacteriuria ( $p > 0.05$ ).

Significant growth of uropathogens was found in 78 patients with asymptomatic bacteriuria (65%). The remaining 42 patients (35%) had dysuria, frequency, worsening incontinence and/or lower abdominal pain. Patients with persistent positive cultures and those on CIC were periodically treated with appropriate antibiotics.

*E. coli* was the commonest organism detected in 72% of positive cultures. *Klebsiella* was found in 12%, *Pseudomonas* in 5%, *Proteus mirabilis* in 5% and other less common organisms in 6% of cultures (Fig. 2).

The most effective antimicrobials against *E. coli* were amikacin, imipenem and nitrofurantoin. The most effective antimicrobial agents against *Klebsiella* were imipenem and amikacin..

## DISCUSSION

Bacteriuria is a common finding in patients with an orthotopic neobladder substitution after radical cystectomy for muscle-invasive bladder carcinoma<sup>8,9</sup>. The question why there

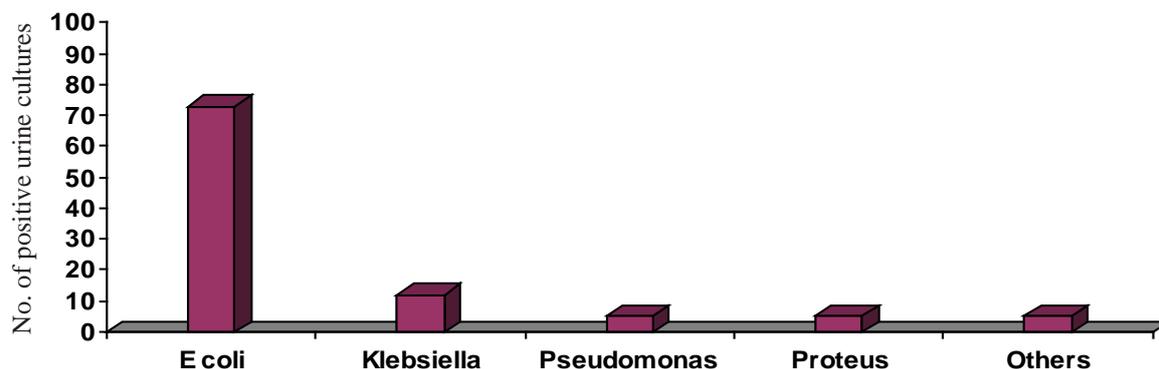


Fig. 2: Type of uropathogens in sigmoid bladder substitution.

is a higher incidence of bacteriuria after radical cystectomy compared to, for example, radical prostatectomy remains a matter of controversy<sup>10</sup>. The normal urothelium has several defense mechanisms against bacteria. Complete voiding is a physically effective action that washes out the bacteria. Most recent experience with bowel neobladder substitution has demonstrated that patients who are able to void well and to empty their neobladder spontaneously generally maintain sterile urine<sup>11</sup>. Consequently, UTI is more commonly encountered in patients requiring CIC<sup>12, 13</sup>.

Most UTIs are caused by facultative anaerobes in the bowel flora. Apart from *E. coli* which is by far the commonest organism, other gram negative organisms such as *Enterococcus faecalis* and *Staphylococcus saprophyticus* are responsible for most community-acquired infections<sup>7</sup>. In our study *E. Coli* was the commonest organism encountered. It has been hypothesized that the intestine, in contrast to the urothelium, is incapable of inhibiting bacterial proliferation. Thus, intestine that normally exists in symbiosis with bacteria with no inflammatory reaction may render the urine less bacteriostatic, promoting bacterial growth and infection<sup>14</sup>. In contrast, Mansson et al showed that the chemical differences in reservoir urine do not promote bacterial growth compared with urine from the native bladder. Another important ob-

servaion is that bacteriuria decreases over time. The mechanism of this acquired defense over time is unknown<sup>15</sup>.

In the present study bacteriuria with sigmoid neobladder substitution was seen in 64%, 47% and 33% at 3, 6 and 12 months, which is comparable to that reported by other authors<sup>5,16,17</sup>. Wullt et al. reported positive urine cultures in 67% of specimens collected from patients with colonic and ileal neobladder<sup>16</sup>.

Abdel Latif et al. reported a higher incidence of positive cultures at the first follow-up visit (74.5%), with a steady decline of bacterial growth to 35.6%, 33% and 6.7% at 6, 12 and 18 months respectively<sup>17</sup>. Wood et al. found positive urine cultures in 50% of patients with intestinal neobladder; they concluded that UTI was the only predictor for urosepsis<sup>5</sup>.

In our study, the isolated bacteria were mainly intestinal species; the most common organism was *E coli* (72%), followed by *Klebsiella* (12%). These findings are similar to the results reported by others<sup>8,16,18</sup>. Keegan et al. found that the *E coli* strains isolated from intestinal reservoirs were less likely to carry determinants of virulence, e.g. P- and S-fimbriae and toxins, compared to community acquired *E coli* strains<sup>18</sup>.

In our study, 65% of the patients with bacteriuria and significant growth of uropathogens were asymptomatic. Iwakiri et al. suggested that the interposed isolated intestinal segment has an innate tolerance, thus providing conditions favoring the asymptomatic carriage of bacteria<sup>10</sup>.

It was found that CIC did not increase the incidence of active UTI in our study. The same finding was reported by Wood et al<sup>5</sup>. CIC facilitates complete emptying of the neobladder, thus decreasing the amount of residual and preventing upper tract dilatation.

There are data supporting the use of prophylactic antibiotics in patients with a neobladder, unless they have significant symptoms or complications, such as elevated PVR, new stones, upper tract obstruction or reflux<sup>8, 17</sup>. Bazzocchi et al. found that oral bacteriotherapy not only modified intestinal microflora but also clinically improved intestinal motility in irritable bowel syndrome in patients with a reconstructed lower urinary tract<sup>19</sup>. This finding may support restriction of antimicrobial therapy to patients with symptomatic bacteriuria and those who are at risk of deterioration of renal function due to UTI. According to Wullt et al. prophylactic antibiotic therapy does not seem to reduce the bacterial burden, but interferes with bacterial composition<sup>16</sup>.

In conclusion, like ileal bladder substitutes the sigmoid neobladder after radical cystectomy is associated with bacteriuria in the majority of patients. As long as bacteriuria is asymptomatic it is not a clinical problem and does not require urgent therapy. Regular follow-up is mandatory and use of prophylactic antibiotics is recommended for patients with lower urinary symptoms and those at risk of developing complicated UTI and impairment of renal function.

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## CLINICAL SIGNIFICANCE OF BACTERIURIA IN PATIENTS WITH ORTHOTOPIC SIGMOID NEOBLADDER

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