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Urosepsis and the urologist!

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Abstract

Introduction: Sepsis is a life-threatening organ dysfunction that is caused by a dysregulated host response to the infection. Urosepsis contributes up to 25% of all sepsis cases. An important part of the management of urosepsis is to rule out possible surgical causes such as urolithiasis, obstructive uropathy, or abscess formation along the urogenital tract.

Objective: The aim of this study is to look at whether urological conditions and recent urological surgery contribute significantly to all patients admitted with urosepsis.

Methods: A total of 2679 urine cultures and 654 blood cultures performed in Connolly Hospital Emergency Department were reviewed between 2016 and 2018. Patients were included if they had a matching urine culture and blood culture performed within 24 hours of admission. A retrospective chart review was performed for all patients included in the study.

Results: Our study included 85 patients admitted with urosepsis between 2016 and 2018. The average age was 70.3 years (21–100 years), in which 61% (n = 52) of patients were female, 18% (n = 16) had a long-term indwelling catheter, 11.8% (n = 10) were admitted as urosepsis with a urological condition. The most common urological condition predisposing patients to urosepsis in this study was bladder outlet obstruction secondary to benign prostatic hyperplasia. A total of 4.7% (n = 4) of patients died during their admission. The complications as a result of urosepsis included a prostatic abscess, a psoas abscess, an ileus, an infected cyst, and 1 case of emphysematous pyelonephritis.

Conclusion: In this study, the majority of patients admitted with urosepsis did not have an underlying urological condition or recent urological instrumentation. Clinicians should be aware of potential complications as a result of a urosepsis.

Keywords: Benign prostatic hyperplasia; Urinary stones; Urinary tract infection; Urology; Urosepsis

1. Introduction

Urosepsis makes up to 25% of all adult sepsis cases admitted to hospital.[1] Septic shock secondary to urosepsis has a high mortality, with 20%–40% of patients dying during their admission.[2] Recently, the incidence of urosepsis has increased, but the associated mortality has declined, suggesting that the early goal-directed management of urosepsis has improved.[3] Urosepsis can present as many different conditions including pyelonephritis, cystitis, renal abscess, perinephric abscess, acute prostatitis, and acute epididymo-orchitis.

An important part of the management of urosepsis is to rule out a possible surgical cause such as urolithiasis, urinary retention, a structural abnormality, or abscess formation along the urogenital tract, as these patients will not improve until drainage of the infected urine or collection is performed. This is best achieved with the use of imaging such as ultrasonography or computed tomography (CT). A Danish study in 2012 reviewed the imaging of 115 patients admitted with bacteremic urosepsis.[4] Major abnormalities were detected in 37 patients. The 2 most common abnormalities were hydronephrosis (17%) and urolithiasis (6%). One study reviewed 93 patients with febrile urinary tract infection (UTI) and recommended ultrasonography in patients with fever for more than 3 days, a previous history of urolithiasis, or patients with diabetes mellitus. However, in this paper, major abnormalities were picked up in 18% of all cases.[5]

A Mexican study reviewed 173 patients admitted with a complicated UTI.[6] A complicated UTI is associated with any condition that increases the probability of acquiring the infection or not responding to the standard treatment. Obstructive uropathy (73.4%) and urinary stone disease (33.5%) were 2 common factors associated with the development of a complicated UTI. Unfortunately, data were not collected on the urological follow-up and management subsequently. A prospective study conducted in Spain reviewed 1325 patients admitted with complicated pyelonephritis. Complicated pyelonephritis was defined as pyelonephritis in "any male patient, in patients with functional or anatomical abnormalities of the urinary tract, immunosuppressed persons, patients with a single kidney, permanent bladder catheter, nephrostomy or double-J catheter, or those patients who had experienced urinary tract manipulation in the previous 2 weeks".[7] Total 70.9% of patients admitted with urosepsis in this cohort had a structural or functional abnormality of the urinary tract, which included benign prostatic hyperplasia (BPH), neurogenic bladder, structurally abnormal bladder, single kidney, and urethral obstruction. In this cohort, 25.5% patients had urolithiasis.

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There has been no study to date that reviewed the incidence of a urological condition in all patients admitted with urosepsis. The aim of this study is to look at whether urological conditions or recent urological instrumentation contribute significantly to all patients admitted with urosepsis and to design an algorithm for management of different causes of urosepsis. A secondary aim is to review the outcomes of patients admitted with urosepsis secondary to a urological condition versus patients admitted with urosepsis with no urological condition.

2. Materials and methods

A total of 2679 urine cultures and 654 blood cultures performed in the Emergency Department of Connolly Hospital Blanchardstown, a 350-bed acute hospital, were reviewed between 2016 and 2018. Urosepsis was defined as any patient with matching urine and blood cultures admitted for the treatment of urosepsis, with 2 more of the systemic inflammatory response syndrome (SIRS) on admission. Patients were included if they had a positive urine culture and blood culture with the same organism, performed within 24 hours of admission. An extensive retrospective chart review was performed for all patients included in the study. Patients were included if they had no hospitalizations in the previous 48 hours. Patients were required to have a minimum of 2 criteria of the SIRS on admission (Fig. 1).[8] Blood and urine culture results were recorded in the excel sheets.

Imaging of the renal tract including ultrasonography, CT, and magnetic resonance imaging of the patients performed during their admission were reviewed to rule out a surgical cause of their urosepsis. As part of the retrospective chart review, any input from the urology team was noted including subsequent follow-up in an outpatient setting.

Multidrug resistant (MDR) organisms were defined as a bacterial isolate that was resistant to 1 or more agents in 3 or more different classes of antimicrobials. The isolate is expected to be susceptible to penicillins, cephalosporins, aminoglycosides, fluoroquinolones, and carbapenems.[9] Patient demographics including age and sex, underlying co-morbidities, length of stay, duration of antibiotic therapy and all-cause mortality were collected.

Vital signs at the time of triage and the initial treatment of urosepsis were evaluated, and lactate was recorded to help determine if patients were in septic shock. Septic shock was defined by the clinical requirements according to the Society of Critical Care Medicine and the European Society of Intensive Care Medicine at the 3rd International Consensus Definitions for Sepsis and Septic Shock.[10]

SIRS criteria – two of the following:

- Temperature > 38°C or < 36°C;
- Heart rate > 90 beats per minute;
- Respiratory rate > 20 or $PaCO_2$ < 32 mm Hg;
- WBC > 12,000/ml, < 4,000/ml, or the presence of > 10% immature neutrophils;
- Altered Glasgow coma scale;
- Blood glucose > 7.7 mmol/l in non-diabetic patients.

Figure 1. SIRS criteria. SIRS = systemic inflammatory response syndrome.

Admissions to the intensive care unit and high dependency unit were also included in the data collection. Data on the initial antibiotics prescribed and any changes to the antibiotics during the admission were also reviewed. All blood results were recorded on admission. Data were exported to Minitab for statistical analysis. The sample *t* test was used to compare age, length of stay, and duration of antibiotics between patients admitted with urosepsis due to a surgical cause versus patients with no underlying etiology. The Fischer exact test was used to compare co-morbidities between the 2 groups.

3. Results

From a total of 2679 urine cultures and 654 blood cultures, our study included 85 patients admitted with urosepsis between 2016 and 2018, in which 61% (n = 52) of patients were female. The average age was 66.6 years (21–100 years) in female patients and 73.8 years (46–92 years) in male patients.

3.1. Pathogens involved in urosepsis

The pathogens identified as causing urosepsis in our study population are illustrated in Figure 2. The most common pathogen was *E. coli*, causing 85.9% (n = 73) of all urosepsis cases. Among the 83 patients admitted with urosepsis due to a gram-negative organism, 7 were classified as being due to the extended spectrum beta lactamase producing organisms and 34.1% (n = 29) of all pathogens were classified as an MDR organism (as defined above).

3.2. Underlying urological conditions

All patients had an imaging of their renal tract with either ultrasonography or CT. The majority of patients had an ultrasound of the renal tract (90%, n = 77), and 11.8% (n = 10) of patients admitted with urosepsis were associated with a surgical condition. The most common urological condition in this study was urinary retention secondary to BPH (n = 4) (Fig. 3). There were 2 patients who subsequently underwent a trans-urethral resection of the prostate (TURP) in an elective setting and had a successful trial without catheter. The other 2 patients were not fit for anesthesia and were managed with long-term urinary catheters. The 3 patients admitted with an obstructing ureteric calculus underwent general anesthesia, and a cystoscopy and insertion of a ureteric stent were performed. Subsequently, a ureteroscopy and lasertripsy were performed 6–12 weeks later to treat the calculus. The final patient was diagnosed with a neurogenic bladder after urodynamics was performed and followed up in the urology outpatient department. This was likely secondary to poorly controlled type 2 diabetes mellitus. This patient was managed with self-intermittent catheterization. In terms of recent urological instrumentation, 1 patient underwent a flexible cystoscopy 2 days previously and the 2nd patient underwent a rigid cystoscopy and insertion of stent for an obstructing ureteric calculus 2 weeks previously. Both were managed with the insertion of a urethral catheter and intravenous antibiotics.

A total of 18% (n = 16) of patients had a long-term catheter, in which 11 patients were elderly gentlemen with dementia from long-term care facilities. This was not considered as a urological condition, as these patients were likely not suitable for a surgical procedure to allow them to be catheter-free due to their co-morbidities. However, due to poor documentation, it was difficult to know the underlying reason for the long-term catheter or when they were last changed.

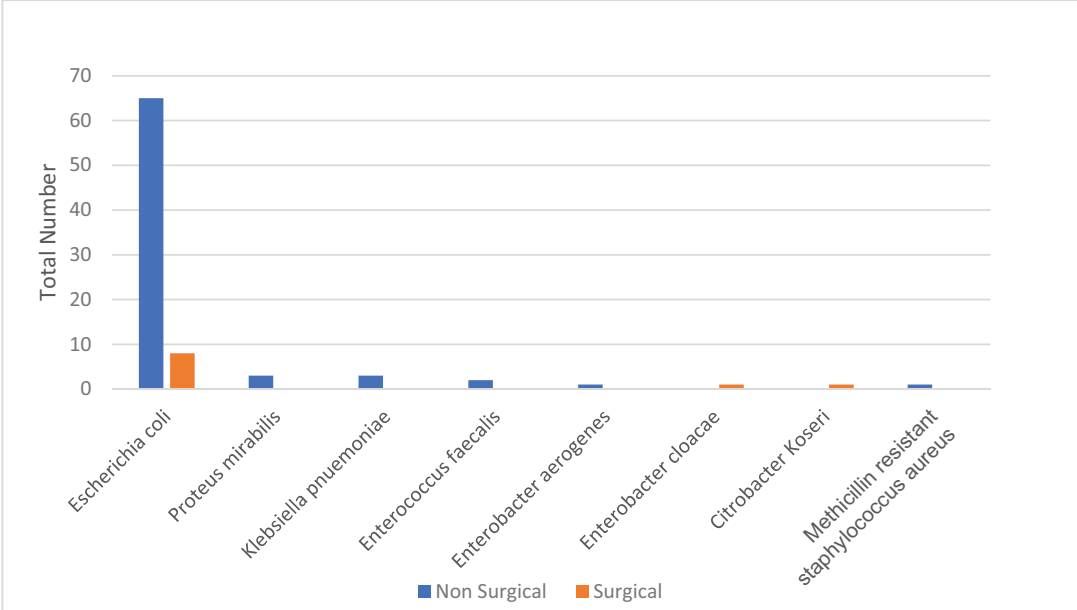

Figure 2. Pathogens causing urosepsis.

3.3. Comparing urological and nonurological causes of urosepsis

In this cohort, 11.8% (n = 10) of the patients had recent urological instrumentation or an underlying urological condition. The average age of patients admitted with urosepsis secondary to a urological condition was 62.9 (± 12.7, 95% CI) compared to 70.44 (± 3.8, 95% CI). In Table 1, patient demographics and co-morbidities were compared between patients admitted with urosepsis secondary to a urological condition versus patients with no underlying urological condition. Although it appears that elderly patients are less likely to have a urological condition, this was not statistically significant and may be related to the small sample size. Similarly, patients admitted with urosepsis appear to have a longer length of stay, however, this was also not statistically significant. There was no difference in co-morbidities between the groups.

3.4. Complications and outcomes

In this cohort, 4 patients (5%) died as a result of urosepsis. The average age of these patients was 78 years (60–93 years). Among

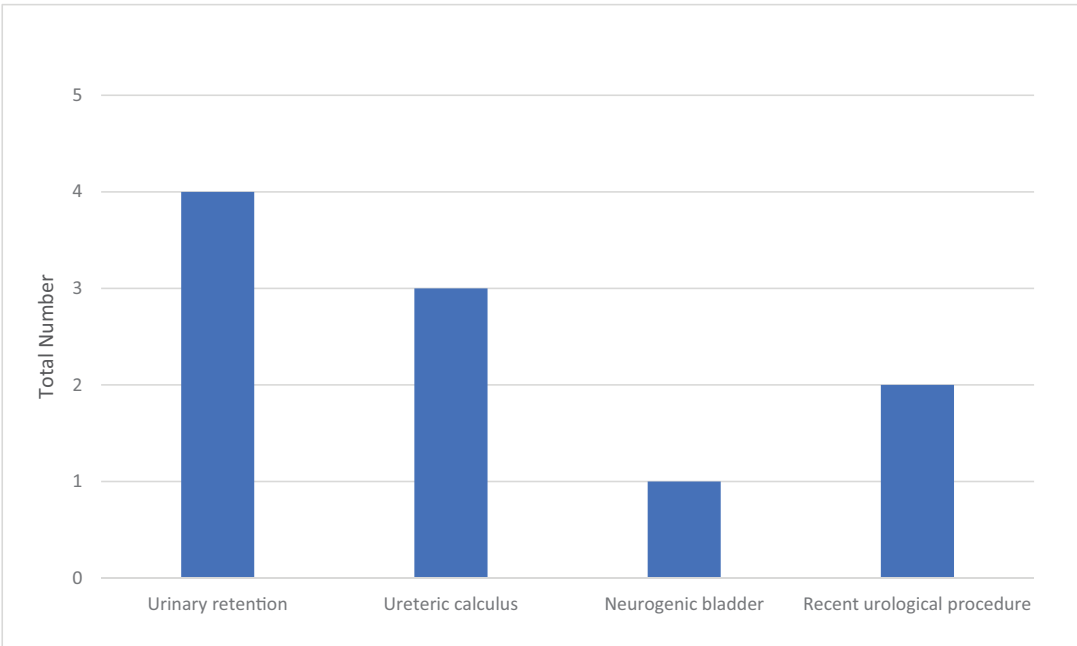

Figure 3. Urological conditions contributing to urosepsis.

Table 1

Comparing urological and nonurological causes of urosepsis.

	Urological	Nonurological	*p*
Total, n	10	75	
Sex, n			0.19
Male	6	28	
Female	4	47	
Age, y	62.9±12.777 (95% CI)	70.44±3.794 (95% CI)	0.2
Average length of stay, d	17.6±13.848	11.8±3.09	0.2456
Duration of antibiotic therapy, d	11.9±1.91	11.3±2.7	0.6
Way of infection, n			0.68
Community acquired	9	58	
Long-term care acquired	1	17	
Co-morbidities, n			
• Diabetes	2	15	1.0
• Dementia	1	14	1.0
• Hypertension	2	34	0.17
• Ischemic heart disease	2	19	1.0
Mortality	0	4	1.0

CI = confidence interval.

them, 3 were female patients presenting in septic shock to the emergency department. The 4th patient was an 83-year-old gentleman with multiple co-morbidities who never returned to baseline after the treatment of urosepsis. The patient had a prolonged hospital stay. Palliative measures were introduced, and the patient died on day 62 of admission. None of these patients were diagnosed with a urological condition during their admission.

There were 3 complications documented as a result of urosepsis. The first was a patient with type 1 diabetes mellitus admitted with urosepsis and urinary retention secondary to BPH. An ultrasound diagnosed a small prostatic abscess. This was managed conservatively with antibiotics, and he subsequently underwent a successful trial without catheter after an elective TURP. The second patient developed emphysematous pyelonephritis after being admitted with urosepsis secondary to a neurogenic bladder related to poorly controlled diabetes mellitus. This was also managed conservatively with a prolonged course of antibiotics. The third patient developed a psoas abscess during her admission with urosepsis. She required an image-guided aspiration of the abscess by radiology and a 4-week course of antibiotics. The final patient developed an ileus during her admission and was managed with a nasogastric tube, and fluids and symptoms were resolved after 4 days.

From a review of the literature and the results from this study, an algorithm was designed to help manage urosepsis secondary to a number of different causes (Fig. 4). Urolithiasis, hydronephrosis and abscess formation along the urogenital tract should have input from the urology service while inpatient.

4. Discussion

In our study, we showed the overall small contribution of urological conditions in all patients admitted to hospital with urosepsis. In our cohort, we found that 10% (n = 11) of all patients admitted with urosepsis had an underlying urological condition or recent urologyical instrumentation. Of note, only 2 patients (2.3%) had recent urological instrumentation, which shows that urology instrumentation contributes very little to patients admitted with urosepsis.

Previous studies have shown that the most common urological condition associated with infections in the urogenital tract was urolithiasis or structural and functional abnormalities, such as BPH or neurogenic bladder.[5,7] In 1990, a study by Serniak et al.[11] reviewed 205 cases of urosepsis and found that 43% of cases were from urolithiasis, 25% from prostatic adenoma, 18% from urological cancer, and 14% from other urological diseases.

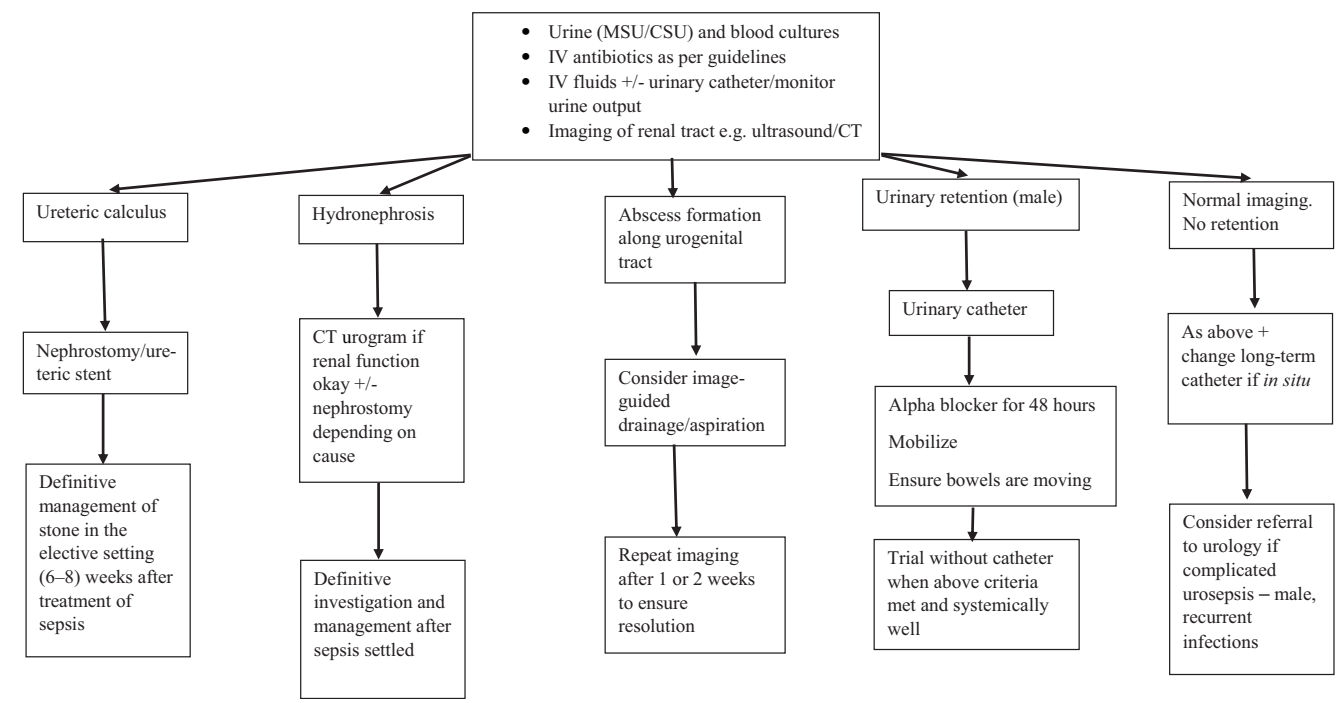

Figure 4. Algorithm for the management of urosepsis. CT = computed tomography; IV = intravenous; MSU = mid-stream urine; CSU = catheter specimen of urine.

This is similar to findings in our study. However, these studies looked at cohorts who were at an increased risk of having an underlying condition such as complicated UTIs or complicated pyelonephritis rather than all patients presenting to hospital with urosepsis. We feel our study gives a good overall understanding of the urological contribution to all patients admitted to hospital with urosepsis. Our most common underlying urological condition in patients admitted with urosepsis was bladder outlet obstruction secondary to BPH. BPH is a part of the aging process in men, with studies quoting that 8% of men have BPH in the fourth decade of life and 90% of men have BPH in the 9th decade of life.[12] Most patients with BPH can be managed with medication in terms of an alpha blocker or 5-alpha reductase inhibitor. In a minority of patients who fail medical management and are fit enough for an operation, a TURP is necessary.

Studies in the past have highlighted the increased risk of developing urosepsis in patients with long-term urinary catheters, and these findings are reiterated in our paper. In this sample, 18% (n = 16) of patients had a long-term urinary catheter. The majority of these patients were elderly gentlemen with dementia from long-term care facilities. It was difficult to ascertain whether these catheters were changed regularly because of the poor documentation and the fact that urinary catheters are changed in different settings. Also, as these urinary catheters had been in for a long period of time, it was difficult to know the underlying etiology or whether the patient had been seen by a urologist prior to deciding that a long-term urinary catheter was necessary. A long-term urinary catheter has been shown to be an independent risk factor for mortality in urosepsis and should be changed if in situ in these patients.[7]

Historically, the most common organism causing urosepsis is *E. coli*, and our data support these studies.[13] In our study, over a third of patients developed urosepsis from an MDR organism. Increasing antimicrobial resistance in patients admitted with urosepsis poses a challenge in prescribing the appropriate antibiotics. Appropriate microbiological samples, prior to antibiotic administration are essential in the treatment of urosepsis, in order to subsequently direct antibiotic treatment. Following local antibiotic guidelines, which should be based on international best practice as well as local epidemiological information, is also important in the early goal-directed management of urosepsis.[14]

There were no difference in outcomes, length of stay, or patient demographics between patients with urosepsis secondary to an underlying condition versus patients with urosepsis with no underlying urological condition. This is likely due to the relatively small sample size. Yamamichi et al.[15] found that patients admitted with urosepsis due to occlusion of the urinary tract were more likely to present in shock compared to patients without occlusion. Few studies have compared outcomes between urosepsis due to an underlying urological condition and urosepsis with no underlying urological condition.

Most cases of urosepsis are secondary to a complicated UTI or pyelonephritis.[6] However, with urosepsis, clinicians should be aware of the risk of abscess formation along the urogenital tract and collections forming in previous cysts. Studies have shown that persisting fever despite adequate antimicrobial cover and patients who have diabetes mellitus or who are immunosuppressed are more likely to develop these complications.[5] Minimally invasive procedures, such as image-guided drainages may be necessary in patients who develop an abscess. In our study, only 1 patient required an image-guided aspiration of a collection. More invasive operations, such as nephrectomy do have a role in cases that do not respond to more minimally invasive procedures or in cases whose drainage of the collection is not possible.[16,17]

Urosepsis is one of the leading causes of severe sepsis and septic shock.[2] In our study, there was an all cause of mortality of 5% (n = 4). Unfortunately, in 20%–40% of cases, shock due to urosepsis leads to death.[14] In this study, nearly 30% of patients presenting with septic shock due to urosepsis died during their admission. It is crucial to recognize urosepsis quickly and to provide early goal-directed treatment, as delayed treatment has shown to result in a 7.6% increase in mortality after the onset of hypotension.[18] According to Hoffman et al, the leading causes of shock in patients with an underlying urological condition were urinary obstruction in 78% of patients and uropathies with significant abnormalities on in urodynamics in 22% of patients.[19]

From a urology point of view, the leading causes of shock in urosepsis in urological patients were urinary obstruction in 78% of the patients and uropathies with significant abnormalites on urodynamics in 22% of the patients. This study has some limitations. It was a retrospective single centre study, therefore, data may not be generalizable to other institutions. Data collection was performed by reviewing patient charts, therefore, it was based on accurate documentation, which was not always reliable. The sample size was relatively small, which may have limited the ability to detect a statistically significant difference between length of stay and patient outcome between patients admitted with urosepsis as a result of an underlying urological condition versus patients admitted with urosepsis with no underlying condition. However, strict inclusion criteria were used, which allowed us to accurately capture a specific patient cohort.

5. Conclusion

In patients admitted to hospital with urosepsis, the majority of patients do not have an underlying urological condition. Patients who have had recent urological instrumentation make up a very small percentage of all patients admitted with urosepsis. Blood and urine cultures prior to antibiotic administration are essential in the treatment of urosepsis because of the high level of antimicrobial resistance. Medical staff should be reminded that long-term catheters predispose patients to a much greater risk of sepsis, and efforts should be made to keep patients free from a long-term urinary catheter for as long as possible and to seek a urology opinion before a decision is made. Clinicians should be aware of possible complications associated with urosepsis, such as abscess formation along the urogenital tract, emphysematous pyelonephritis, and ileus. Future studies should look at the prevention of urosepsis and the risk factors associated with developing a complication from urosepsis.

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Statement of ethics

Ethical approval was not required as per the local ethics committee given this was a retrospective study with anonymised

data. The study was performed in accordance with the World Medical Association Declaration of Helsinki.

Conflict of interest statement

The authors declare that they have no financial conflict of interest with regard to the content of this report.

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None.

Author contributions

JR, LMcL and EON conceived and designed the study, performed the statistical analysis and wrote the paper. JR collected the data.

References

[1] Wagenlehner FM, Weidner W, Naber KG. Optimal management of urosepsis from the urological perspective. *Int J Antimicrob Agents* 2007;30(5):390–397.
[2] Wagenlehner FM, Lichtenstern C, Rolfes C, et al. Diagnosis and management for urosepsis. *Int J Urol* 2013;20(10):963–970.
[3] Brun-Buisson C, Meshaka P, Pinton P, Vallet B. EPISEPSIS Study GroupEPISEPSIS: a reappraisal of the epidemiology and outcome of severe sepsis in French intensive care units. *Intensive Care Med* 2004;30 (4):580–588.
[4] Sorensen SM, Schonheyder HC, Nielsen H. The role of imaging of the urinary tract in patients with urosepsis. *Int J Infect Dis* 2013;17(5): e299–e303.
[5] Wang IK, Chang FR, Yang BY, Lin CL, Huang CC. The use of ultrasonography in evaluating adults with febrile urinary tract infection. *Ren Fail* 2003;25(6):981–987.
[6] Cornejo-Dávila V, Palmeros-Rodríguez MA, Uberetagoyena-Tello de Meneses I, et al. Management of complicated urinary tract infections in a referral center in Mexico. *Int Urol Nephrol* 2015;47(2):229–233.
[7] Buonaiuto VA, Marquez I, De Toro I, et al. Clinical and epidemiological features and prognosis of complicated pyelonephritis: a prospective observational single hospital-based study. *BMC Infect Dis* 2014;14(1): 639.
[8] Simpson SQ. SIRS in the time of sepsis-3. *Chest* 2018;153(1):34–38.
[9] The Royal College of Physicians Clinical Advisory Group on Healthcare Associated Infections: Guidelines for the prevention and control of multi-drug resistant organisms (MDRO) excluding MRSA in the healthcare setting. Available from: http://hdl.handle.net/10147/303397. Accessed January 7, 2019.
[10] Singer M, Deutschman CS, Seymour CW, et al. The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3). *JAMA* 2016;315(8):801–810.
[11] Serniak PS, Denisov VK, Guba GB, et al. The diagnosis of urosepsis. *Urol Nefrol (Mosk)* 1990;(4):9–13.
[12] Langan RC. Benign prostatic hyperplasia. *Prim Care* 2019;46(2): 223–232.
[13] Rosenthal EJ. Epidemiology of septicaemia pathogens. *Dtsch Med Wochenschr* 2002;127(46):2435–2440.
[14] Wagenlehner FME, Pilatz A, Weidner W, Naber KG. Urosepsis: overview of the diagnostic and treatment challenges. *Microbiol Spectr* 2015;3(5). doi: 10.1128/microbiolspec.UTI-0003-2012.
[15] Yamamichi F, Shigemura K, Kitagawa K, et al. Shock due to urosepsis: a multicentre study. *Can Urol Assoc J* 2017;11(3-4):E105–E109.
[16] Hung CH, Liou JD, Yan MY, Chang CC. Immediate percutaneous drainage compared with surgical drainage of renal abscess. *Int Urol Nephrol* 2007;39(1):51–55.
[17] Lin WC, Chen YF, Lin CH, et al. Reappraisal of the management and outcome of emphysematous pyelonephritis. *Kaohsiung J Med Sci* 2009;25(1):16–24.
[18] Kumar A, Roberts D, Wood KE, et al. Duration of hypotension before initiation of effective antimicrobial therapy is the critical determinant of survival in human septic shock. *Crit Care Med* 2006;34(6):1589–1596.
[19] Hofmann W. Urosepsis and uroseptic shock. *Z Urol Nephrol* 1990;83 (6):317–324.

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