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MICROBIOLOGICAL TRENDS AND CLINICAL MANAGEMENT OF UROSEPSIS IN A TERTIARY HOSPITAL IN NIGERIA: A RISK-BASED APPROACH

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Abstract: Background; Urosepsis is a common urologic emergency due severe urogenital tract infection. It is associated with a high mortality rate of 25-60% worldwide. Urinary tract obstruction and presence of indwelling catheter/ stent are the commonest risk factors. Aggressive management is associated with good outcome. No previous study done in our environment. We studied presentation, risk factors, microbiological pattern and management of urosepsis in our hospital.
Methods: This is a retrospective study of patients managed for urosepsis by the Urology Unit, of our hospital from January to December
2017. All urological patients with genito-urinary infection that fulfil systemic inflammatory response criteria were included. Patients who did not fulfil the criteria or have incomplete data were excluded. Data was collected via a proforma and analyzed using SPSS version 25.0 for windows. Data collected include biodata, clinical, laboratory, imaging findings, treatment and outcome. Results were reported in percentages and mean ± standard deviation.
Results: There were 77 patients with urosepsis within the study period, with mean age of 50.9 ± 21.1 years and a range of 1 to 80 years. The male to female ratio was 4:1. The patients' presentations were fever (68.8%), lower urinary tract symptoms (51.9%), weight loss (35.1%), anorexia (29.9%), hematuria (29.9%) pyonephrosis (13%) and vomiting (7.8%). The most common risk factors for the urosepsis were urinary tract obstruction + indwelling catheter/ stent (93.2%), complicated genito-urinary infection (4.2%) and immunosuppressive medical conditions (2.6%). The microbiological pattern included Escherichia coli in 45 patients (58.4%), Staphyloccus aureus and Klebsiella spp in 2 patients (2.6%) each. Candida albicans was found in 1 patient (1.3%). All patients had parenteral antibiotics, fluid therapy with normal saline ± blood transfusion and monitoring. The recovery and mortality rate were 93.5% and 3.9% respectively.
Conclusion: Urosepsis present with local and systemic symptoms in patients with urinary tract obstruction, indwelling urethral catheter, urogenital infections and immunosuppression. Escherichia coli, Staphylococcus aureus and Klebsiella spp were most common organisms involved. Aggressive management is associated with a good outcome.
Keywords: Pathogens, Risk factors, Schistosomiasis, Ureteral obstruction, Urinary bladder neck obstruction, Urosepsis.

INTRODUCTION

Urosepsis is a life -threatening organ dysfunction caused by dysregulated host response to infection originating from the urinary tract and or the male genital organ.[1] Urosepsis is a form of severe sepsis in which there is organ dysfunction[2.] It accounts for 10-30% of severe sepsis [2]and carries a high mortality of 25-60% worldwide.[1,3] It is therefore best prevented than treated[1] It can be prevented by aseptic techniques, appropriate use of prophylactic and therapeutic antibiotics and short hospital admission before surgery to reduce nosocomial urosepsis.[1] Early

removal of catheter and stents will also go a long way in reducing the infection.[1] Urinary tract obstruction and other forms of urogenital tract infection are the most common risk factors for urosepsis [4.] Complicated uro-genital tract infections such as obstructive pyelonephritis, pyonephrosis, epididymo-orchitis, Fournier's gangrene and catheter or stent associated urinary tract infection (CAUTI), are form of infections which may progress to urosepsis if not appropriately managed.[5] Other risk factors include advanced age, immunosuppressive medical conditions such as diabetes mellitus and retroviral disease. [6,7] The most common causes of urinary tract obstruction in our environment include BPH, urethral stricture, schistosomal ureteric obstruction and urolithiasis.[8] The management involve early diagnosis, early parenteral antibiotics administattion, fluid therapy ± blood transfusion and identification and elimination of the risk factors by change of catheter or removal of a stent and drainage of pyonephroisis.[1,8] There is no study done on urosepsis or urinary tract infection in urological patient in our environment. The studies done on UTI are laboratory based, [9,10,11] hence the need for the present study.We study presentation, risk factors, microbiological pattern and management of urosepsis in a tertiary hospital in Northwestern, Nigeria.

METHODS

This was a descriptive retrospective study of consecutive patients managed for urosepsis at the Urology Unit of our hospital from January to December 2017. All patients with clinical diagnosis of urogenital infections that fulfilled at least two Systemic Inflammatory Response Syndrome (SIRS) criteria [9] (appendix A) were included in the study. Patients that did not fulfil the SIRS criteria or with incomplete records were excluded from the study. Patients were managed based on the protocol below. Data was collected via proforma and analyzed using SPSS version 25.0 for windows. The Results were reported in percentages and mean ± standard deviation. The information collected include biodata, clinical data, results of laboratory investigations, findings of imaging studies, treatments and outcome. Urosepsis is defined as documented urogenital infection with SIRS and organ dysfunction as in appendix A. Catheter/ stent associated UTI (CAUTI) is defined as pyuria ± symptoms in patient with indwelling catheter or stent greater than 10 days. Urinary tract infection is defined as significant pyuria with positive culture in patients not antibiotics or with or without positive culture in patients on antibiotics. Significant pyuria is present when there are pus cells > 5/ HPF. Good outcome signifies recovery and discharge from the hospital. Poor outcome is when there is mortality or patient left against medical advice. This study was approved by Health Research and Ethical Committee of our Hospital.

Protocol for the management of urosepsis

Patients with urological conditions that fulfil the SIRS criteria were admitted. large bore cannulae were inserted and patients were resuscitated with normal saline ± blood. Samples of urine and blood were taken for laboratory investigations. Empirical intravenous antibiotics were commenced within 1 hour of the diagnosis. These included; ceftriaxone/sulbactam with or without gentamicin and metronidazole depending on the predisposing urological condition and renal function. Abdominopelvic ultrasound ±transrectal ultrasound was done to identify the focus of infection which was removed under ultrasound guidance when there is suppuration. Samples of urine and pus were taken for microscopy and sensitivity. Urethral or suprapubic catheter changed when present and tip was sent for microscopy and sensitivity. Ureteric stent was removed when present. Bladder irrigation with 10% povidone iodine was done in patients with obstructive pyuria. Vital signs, urine output were monitored regularly. In patients with Fournier's gangrene serial debridement of wound, hypertonic saline bath, triple antibiotics (ceftriaxone, gentamicin, metronidazole) and wound dressing using 10% povidone iodine were done. Tissue was sent for

histology and microcopy if feasible. Consultant microbiologist and plastic surgeon were involved where necessary.

RESULTS

There were 77 patients managed for urosepsis within the study period with mean of age 50.9 ± 21.1 years and a range of 1 to 80 years. There were 61 males (95.2%) and 16 females (4.8%) with a male to female of 4:1.

The most common presentations were fever in 53 patients (68.8%) and lower urinary tract symptoms (LUTS) in 40 patients (51.9%). Other details of the presentations are shown in Figure 1.

The commonest risk factor for urosepsis was urinary tract obstruction and indwelling catheter in 71 patients (93.5%). Other details of the risk factors are shown in Figure 2.

The details of the BOO, UTO and UGI are shown table 1 below. There was indwelling catheter or stent in 62 patients (80.5%) for greater than 10 days leading to catheter/ stent associated urinary tract infection (CAUTI) in the patients. The patients had pyuria and or positive urine culture.

Laboratory investigations revealed pyuria ± nitrituria in 77 patients (100.0%), elevated urea/ creatinine in 37 patients (48.1%), anemia in 26 patients (33.8%) and leukocytosis in 20 patients (26.0 %). Abdominopelvic ultrasound revealed hydronephrosis in 26 patients (33.8%), enlarged prostate in 24 patients (31.2%), pyonephrosis in 10 patients (13%) and renal stone in 3 patients (3.9%).

The commonest uropathogen responsible for the urosepsis was *Escherichia coli* in 45 patients (58.4%). Other details of the microbiological pattern are shown in Figure 3 below

All the patients were resuscitated with normal saline, 30% of the required fluid was given as bolus in an hour, intravenous antibiotics were given based on the protocol above. Blood was given in 5 patients (6.5%) due to anemia. The commonest treatment offered was change of catheter with or without 10% povidone iodine bladder irrigation in 62 patients (80.5%). The bladder irrigation is done when there is intermittent catheter blockage.

Other details of the treatment are as shown in Table 2 below.

There was full recovery in 72 (93.5%), 3 patients (3.9%) had mortality and 2 patients (2.6%) left against medical advice. The median duration of admission was 10 days with a range 7-22 days.

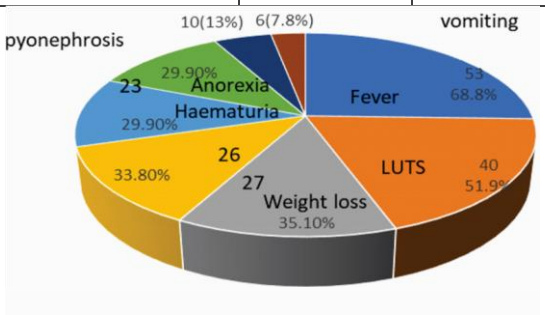
Table 1: Causes of urinary tract obstruction and urogenital tract infection.

Diagnosis	Number of patients		Percentage (%)
BOO 56			**72.7**
BPH	24		31.1
Stricture	12		15.6
Bladder cancer	8		10.4
Neurogenic bladder	3	2	3.9
Prostate cancer	2		2.6
Posterior urethral valve	2	1	2.6
Cystocele	1	1	2.6
Bladder extrophy	1		1.3
DSD	1		1.3
Intraperitoneal bladder rupture	1		1.3
			22.1
UTO 17	10		13.0
	3		3.9
	2	1	2.6
	1		1.3
SUO	3		**5.2**
Renal stone	1		3.9
Endometriosis			1.3
Cervical cancer			
Ureteric ligation			
UGI 4			**100.0**
Fournier's gangrene			
Epididym-orchitis			
Total 77			

Key: schistosomal uretric obstruction (SUO), disorders of sexual differentiation (DSD).

Table 2: Treatment of patients with urosepsis

Treatment	Number of patients	Percentage
Resuscitation (ceftriaxone, fluid)	77 62	100.0 80 .5
Change of catheter	10	13.0 6.5
Percutaneous nephrostomy	5 3	3.9 1.3
Blood transfusion	1	
Wound debridement/ dressing		
DJ Stent retrieval		



Figur e 1: pr esentation of patients with ur osepsis

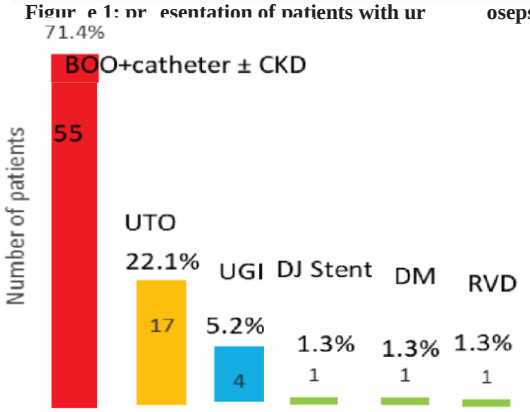


Figure 2: Risk factors for urosepsis.

Key: BOO= Bladder outlet obstruction, CKD= Chronic kidney disease, UTO= Upper urinary tract obstruction, UGI= Urogenital infection, DM= Diabetes mellitus, RVD= Retroviral disease, DJ stent= Double J stent

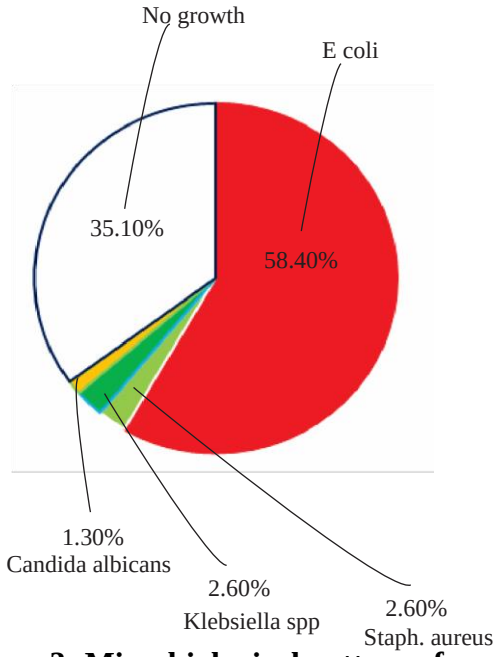


Figure 3: Microbiological pattern of urosepsis

DISCUSSION

Urosepsis is a life-threatening organ dysfunction caused by dysregulated host response to urogenital infection.[1] Presence of obstruction and catheter/ stent are important and frequent risk factors for urosepsis.[1,2] The mortality rate from the infection is as high as 60%[12] Early diagnosis and appropriate treatments are necessary to prevent organ failure and mortality.[12] Appropriate treatments of complicated urinary tract infections (UTIs) and use of antibiotic prophylaxis in patients with indwelling catheter/ stent offers the best chance for prevention and treatment of urosepsis.[7,13] These are however difficult in most African health countries in semi-urban and rural areas due poor accessibility or affordability of the required treatments and lack of skilled manpower in the urban areas. Patients may have to travel long distance to assess such services at secondary or tertiary hospitals in the urban areas.

In 2017 there were 173 urological emergencies in our hospital out of which 77 patients (44.5%) had uroseps which made it the commonest secondary urological emergency as it occurs in setting of other emergencies such as obstruction and urogenital infection.

The mean age of the patients in this study of 51 years is higher than 33 years reported by Odoki *et al* [9] in Bushenyi, Uganda but lower than a range of 67.2 to 83.6 years reported in the western world.[1,14,15] This is due to higher life expectancy with significant number of elderly people in the western world as opposed to what is obtainable in African countries where the life expectancy is low and the population is young. The finding of more men with urosepsis is contrary to what was reported in literature that urosepsis is more common in women [11,15,30]. However, it is consistent with a previous study[17.] The higher prevalence of disease such as BPH, stricture and schistosomal ureteric obstruction in men may explain the disparity. Female with genital and some urinary tract infections may be seen by urogynaecologist and family physicians.

Our patients presented with fever, LUTS, hematuria, weight loss, pyonephrosis and anorexia which is in keeping with what was reported in the literature.

The commonest predisposing factor for the urosepsis was urinary tract indwelling catheter/ stent on background

obstruction. This which was found in 93.2% of the patients as reported by the previous studies. [18,19 20,21] In adult male, BPH, stricture and bladder cancer were the causes of lower tract obstruction [17,22,23] while schistosomal ureteral obstruction was the commonest cause of upper tract obstruction as reported by a previous study [8.] In women cystocele was the commonest cause of lower tract obstruction while endometriosis and ureteric injuries/ ligation were the causes of upper tract obstruction as reported in the literature. [12,24,25] In children PUV, bladder extrophy and DSD were the cause as reported by previous studies. [7,20,26] In 9% of the patients the infection arises primary from the urogenital tract which progress to urosepsis due inability diagnose it early and failure to commence appropriate antibiotics in time. This is common in most African countries due poor health systems and out of pocket payment for medical bills.[18] This can be reverse by health insurance which is not available for informal sector. This can be introduced to cover the poor selfemployed populace. Some patients had Diabetes Mellitus and Retroviral disease which is in keeping with the previous studies.[7,27] This lower the immunity of the patients predisposing them to the sepsis. The urosepsis lead to anemia and uremia in 34% of the patients which is consistent with studies in Africa as patient present to hospital only when complications set in.[18,27,28] These are consistent with chronic kidney disease due to long standing obstruction.

The commonest organism isolated was *Escherichia coli* (58%) as reported by the previous studies.[1,18,20,29] Other organisms isolated were *Klebsiella spp, Staphylococcus aureus and Candida albicans*. This is keeping with previous studies.[17,30] In Fournier's gangrene which is polymicrobial synergistic infections multiple organisms are involved which include gram positive, gram negative bacteria and anaerobes.[11,14,29] There is significant number of negative cultures recorded due prior use of antibiotics. Most patient in low resource setting were started on antibiotics by chemist or health practitioners before presenting to hospital. This will yield negative culture or sterile pyuria. The clinical microbiologist was helpful in deciding the choice of antibiotics in this circumstance more especially when patient is not responsive to ceftriaxone/ sulbactam.

The patients were resuscitated with normal saline, 30% of the requirement given as bolus. Prompt empirical antibiotic therapy with ceftriaxone-sulbactam which was effective in more than 95% of the patients.[17,23,30] Patients vital signs and urine output are monitored hourly by our younger doctors to asses response this is due to in availability or in adequately trained nurses to handle the patients. This care is only available in our intensive care unit. But close clinical monitoring has been rewarding though tedious and time consuming. This equipped our younger doctors more especially the interns with the requisite skill to perform excellently when posted to rural hospital during their youth serve or as medical officers after the mandatory one-year service to nation.

Catheter was changed in 80% of the patients and nephrostomy was passed in 13.0% of patients as reported by previous studies. [1,3,31] This help to remove the source of infection leading to early resolution of symptoms.[1] Patients with indwelling urethral and suprapubic catheters were changed fortnightly and monthly or even earlier if there is pyuria or blockage. This will prevent against development of CAUTI and subsequent urosepsis.[23] This may still develop in patients with immunosuppression or diabetes. Invariably without prophylaxis all patient on catheter develop bacteriuria in10 days. More than 90% of the patients had catheter in situ for up to 30 days leading to catheter associated UTI (CAUTI) as reported in the literature.[32,33] The rate of infection of indwelling catheter is 10% per day.[30] Invariably all catheterized patients will have minimum asymptomatic catheter associated bacteriuria when catheterized for 10 days if they are not on antibiotics. Patients with Fournier's gangrene had serial debridement, triple antibiotics therapy and supportive therapy as reported in the literature.[133] We also

offered the hypertonic saline bath which substitute of hyperbaric oxygen in poor resource setting. This will reduce tissue edema, desiccate microbes, allow tissue to demarcate thereby improving wound healing and control of the infection.

The recovery of 93.5% of the patients was due to early diagnosis and prompt treatment with potent broad spectrum antibiotics therapy as reported in the literature.[17,32] The mortality of 3.9% is lower than what was reported in the western world due to younger population and fewer commodities among the urosepsis patients. [6,34] The range of hospital admission was between 7-22 days which is comparable to the 14-21 days reported previous studies [3,15,20]. Most patients had indwelling catheter which was changed. This led to early resolution of the sepsis when the appropriate antibiotic and supportive treatments were administered. Therefore, is feasible to discharge a patient after a week.

Limitations of this study include those limitations inherent to retrospective study. Records of some data was not adequate. Some patients are on antibiotics so the culture results were negative. Some patients left against medical advice which assessment of their outcome as poor prognosis may not be accurate.

CONCLUSION

Urosepsis is a common urological emergency in patients with urinary tract obstruction, urogenital infection, indwelling catheter or stent and immunosuppressive conditions. It presents with systemic and local urogenital symptoms. The commonest causative organism is *Escherichia coli*. Aggressive management with early empirical antibiotics therapy, fluid resuscitation ± blood transfusion and urinary diversion when indicated are associated with good outcome.

Conflict of interest

The author(s) have no competing interest to declare.

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