Original Research Article

To study the microbiological profile of urosepsis in CKD patients and its treatment

Dushyant B Pawar[1*], Vinayak R Bhoi[2], Shital D Pawar[3], Dilip R Patil[4]

[1]Associate Professor, Department of Medicine, JMF's ACPMMC Dhule, Maharashtra, India
[2]Senior Resident, Department of Medicine, Bharati Vidyapeeth Medical College, Pune, Maharashtra, India
[3]Tutor DPB, Department of Community Medicine, JMF's ACPMMC Dhule, Maharashtra, India
[4]Professor and Head, Department of Medicine, JMF's ACPMMC Dhule, Maharashtra, India

Received: 11-10-2021 / Revised: 26-11-2021 / Accepted: 21-12-2021

Abstract

Introduction: Prevalence of Chronic Kidney disease is increasing worldwide, owing to many associated factors like lower urinary tract obstruction, urinary stones, co-morbidities, and sepsis/ sepsis of urogenital tract. Various parameters like blood pressure, sugar, kidney function tests etc need to be monitored. As urosepsis in CKD has high mortality it is necessary that causative organisms of sepsis should be identified early and antibiotic sensitivity determined to identify resistant organisms. Hence this study was carried out to. **Aim and Objective:** To study the microbiological spectrum involved in urosepsis of CKD patients. To study the treatment of urosepsis in CKD patients. **Materials and methods:** A total of 100 CKD patients were included in the study**,** history and clinical examination was done and blood and urine samples sent to microbiology lab. After culture sensitivity empirical treatment was accordingly changed and results observed. **Results:** *E.coli* was the commonest organism isolated in blood and urine culture. *Candida* was the most common organism responsible for mortality. Cefeperozone-sulbactum and meropenem were the commonly used antibiotics to which patients responded. **Conclusion:** Microbiological investigations in the form of blood and urine culture are of paramount importance in early diagnosis of urosepsis in CKD patients and aids in accurate administration of antibiotics.

Keywords: E.coli, urosepsis, CKD, Antibiotics

Introduction

Chronic Kidney Disease (CKD) encompasses a spectrum of different pathophysiologic processes associated with abnormal renal function & progressive decline in Glomerular Filtration Rate (GFR)[1]. Todi S, et al. (2007) and Mohan A, et al. (2015) described sepsis as a systemic, deleterious host response to infection leading to severe sepsis (acute organ dysfunction secondary to documented or suspected infection) and septic shock (severe sepsis and hypotension not reversed with fluid resuscitation) and reported that mortality of severe sepsis is above 50%[2,3].

Brunkhorst FM (2006) mentioned that urosepsis is a sepsis caused by urinary tract infection (UTI)[4]. Wagenlehner FM, et al. (2013) stated that sepsis which derives from a urogenital tract infection is an urosepsis and it is a common entity that has been documented since long time[5]. Brun-Buisson C. (2000) stated that in 20%–30% of sepsis patients, urinary tract is the most common source of infection, and urosepsis often develops from urinary tract infections (UTIs) acquired in a community or hospital[6]. The severity of urosepsis is closely related to a patient's immune function as other types of sepsis.

Johansen TE, et al. (2007) mentioned that in patients with nosocomial UTI treated in urology departments, the prevalence of urosepsis was, on average 12%[7]. Bouza E, et al. (2001) discussed that in patients with nosocomial UTI treated in other specialties the prevalence for severe sepsis was 2% and for septic shock 0·3%[8]. Hotchkiss RS, et al. (2003) and Brunkhorst FM (2006) discussed that UTIs accounting for mortality due to severe sepsis is approximately 5%[9] to 7%[4]. Hotchkiss RS, et al. (2003) discussed that sepsis from urinary tract generally having a lower mortality than that from other sources[9].

*Correspondence
Dr. Dushyant B Pawar
Associate Professor, Department of Medicine, JMF's ACPMMC Dhule, Maharashtra, India.
E-mail: drdushyantpawar@gmail.com

Wagenlehner FM, et al. (2008) discussed that patients affected by micro-organisms are capable of inducing inflammation within the urinary and male genital tract[10].

Etiology of urosepsis

Wagenlehner FM, et al. (2007) discussed etiology of urosepsis. Gram-negative bacilli account for majority of the cases of urosepsis[11]. Wagenlehner FM, et al. (2007) in their study mentioned that Gram-negative bacilli include Escherichia coli (50%), Proteus spp. (15%), Enterobacter and Klebsiella spp. (15%), and Pseudomonas aeruginosa (5%) which dominate the bacterial spectrum in urosepsis, while Gram-positive organisms are involved less frequently (15%)[11]. Urosepsis is a consequence of urinary tract infection and Enterobacteria are the most common pathogens-

a) Escherichia coli (52%);
b) Proteus species;
c) Enterobacter species;
d) Klebsiella species;
e) Pseudomonas aeruginosa;
f) Gram-positive bacteria, such as enterococci (5%)[12].

Cek M, et al. (2014) and Tandogdu Z, et al. (2016) stated that the rate of sepsis due to fungal organisms has increased and Gram-positive bacteria have become predominant pathogen overall whereas in urosepsis Gram-negative bacteria remains predominant[13,14]. Cardoso T, et al. (2008) mentioned that European Study Group on Nosocomial Infections (ESGNI-004) reported that Gram-positive organisms represented 21.2% of all hospital-acquired UTI, whereas Gram-negative organisms accounted for 65.9% and yeasts 12.9%[15]. Cardoso T, et al. (2008) also mentioned that ESGNI-004 found that in the catheterized patients *Candida* species and P. aeruginosa were more common while E. coli being the commonest bacterium isolated in both catheterized and non-catheterized patients[15]. Tandogdu Z, et al. (2016) mentioned that E. coli remains the most prevalent micro-organism. In several countries, bacterial strains can be resistant or multi-resistant and therefore difficult to treat[14].

Treatment of urosepsis in CKD patients

Dellinger RP, et al. (2012) and Howell MD, et al. (2017) discussed management of sepsis and septic shock. Initial empiric antimicrobial therapy should provide broad antimicrobial coverage against all likely causative pathogens and should be adapted on the basis of culture results, once available[16,17]. In supportive treatment, patient require IVF with Inotropic support, hemodialysis, ventilatory support and few require further urological intervention.

Also, prudent use of antimicrobial agents for prophylaxis and treatment of established infections, to avoid selection of resistant strains. Antibiotic agents should be chosen according to the predominant pathogens at a given site of infection in the hospital environment.

It is crucial to recognize urosepsis rapidly and to provide timely effective treatment, as delay increases the chances of mortality. Hence, this study was conducted to determine the microbiological spectrum of urosepsis in CKD patients and the treatment outcome.

Aim and Objectives

1. To study the microbiological spectrum involved in urosepsis of CKD patients.
2. To study the treatment of urosepsis in CKD patients

Material and Methods

The present study was conducted in the department of general medicine in dialysis unit of a tertiary care hospital from October 2016 to October 2018 to evaluate the patients of urosepsis with chronic kidney disease. It was conducted on 100 patients of chronic kidney disease suffering from urosepsis who were subjected to detail clinical and laboratory evaluations.

The Inclusion Criteria was patients more than 18 year of age, male & female patients who gave valid informed written consent for the study and patients fulfilling the Kidney Disease Improving Global Outcome (KDIGO 2012) criteria for Chronic Kidney Disease (CKD). Patients less than 18 year of age and HIV, HBsAg, HCV Positive patients were excluded from the study.

All the routine blood tests were performed and samples sent to pathology and biochemistry laboratories respectively. To detect bacteremia, samples were sent for blood and urine cultures to microbiology laboratory. The samples were processed for the presence of any microorganism on blood agar, MacConkey agar and chocolate agar. For urine culture, mid-stream urine sample was collected in sterile containers & sent to the microbiology laboratory & processed within 1hr. Common culture media used for bacterial growth was CLED medium while for the fungal growth Sabouraud's dextrose agar was used. Blood samples were sent for testing of HBsAg, HIV and HCV.

HBsAg testing was done by rapid chromatographic immunoassay for the qualitative detection of Hepatitis B Surface Antigen. HCV by Dot immunoassay for detection of antibody to HCV and HIV 1 & 2 was done by Dot immunoassay for detection of antibody to HIV.

The data was coded and entered into Microsoft Excel spreadsheet. Analysis was done using SPSS version 20 (IBM SPSS Statistics Inc., Chicago, Illinois, USA) Windows software program. Descriptive statistics included computation of percentages, means and standard deviations. The unpaired t test (for quantitative data to compare two independent two groups) was used for quantitative data comparison of all clinical indicators. Chi-square test and fisher exact test were used for qualitative data whenever two or more than two groups were used to compare. Level of significance was set at P value ≤ 0.05.

Results

The findings of blood and urine cultures along with treatment given is enlisted in the tables below,

Table 1: Organisms isolated on blood culture in study subjects

Organism	Frequency	Percent (%)
E. coli	38	38.0
Sterile	23	23.0
Proteus	8	8.0
Klebsiella	7	7.0
Polymicrobial	7	7.0
Pseudomonas	7	7.0
CONS	4	4.0
Staphylococci	2	2.0
Streptococci	2	2.0
Candida	1	1.0
Enterobacter	1	1.0
Total	100	100.0

On blood culture, most common pathogen isolated was *E. coli* i.e. 38%, 23% cultures were sterile, 8% had colonies of *Proteus*, 7% shown *Pseudomonas*, *Klebsiella* and Polymicrobial colonies each. CONS was isolated in 4% patients, while staphylococci and *Streptococci* growth was observed in 2% each, 1% patient's blood culture shown growth of *Enterobacter* and *Candida* each. Table 2 shows organisms isolated on urine culture.

Table 2: Organisms isolated on urine culture in study subjects

Organism	Frequency	Percent (%)
E. coli	52	52.0
Proteus	11	11.0
Klebsiella	10	10.0
Pseudomonas	8	8.0
CONS	5	5.0
Acinetobacter	3	3.0
Candida	3	3.0
Enterobacter	3	3.0
Sterile	3	3.0
Polymicrobial	2	2.0
Total	100	100.0

Out of total 100 patients urine culture maximum growth of 52% of E. coli was seen, 11% had growth of Proteus, while Klebsiella and Pseudomonas growth was observed in 10% and 8% patients respectively. 5% patient's urine culture had growth of CONS, other organism

Acinetobacter, Candida, Enterobacter growth in urine culture was seen in 3% study subjects each. 3% patients had sterile urine culture report, while Polymicrobial growth was seen in 2% patients. Table 3 shows Empirical antibiotic administered to study subjects.

Table 3: Empirical antibiotic administered to study subjects.

Antibiotic	Frequency	Percent (%)
Cefo-Sulb	64	64.0
Meropeneme	18	18.0
Cephalexin	14	14.0
Cefo-Sulb + Fluconazole	1	1.0
Cefo-Sulb + Voriconazole	1	1.0
Imipeneme	1	1.0
Pip-Taz	1	1.0
Total	100	100.0

In our study out of total 100 CKD patients, in empirical treatment maximum patients 64 (64%) were treated with Cefo-Sulb, f/b 18 (18%) patient were treated with Meropenem, f/b 14 (14%) were treated with Cephalexin f/b 1 (1%) each were treated with Imipeneme, Pip-Taz, Cefo-sulb with fluconazole, and Cefo-Sulb with Voriconazole to treat urosepsis till discharge.

Table 4 shows Antibiotic sensitive to organism administered to study subjects.

Table 4: Antibiotic sensitive to organism administered to study subjects.

Antibiotic	Frequency	Percent (%)
Cefo-Sulb	40	40.0
Meropenem	27	27.0
Pip-Taz	10	10.0
Imipenem	8	8.0
Cephalexin	7	7.0
Levofloxacin	4	4.0
Ceftriaxone	2	2.0
Fluconazole	2	2.0
Total	100	100.0

In our study out of total 100 CKD patients, according to culture and sensitivity, maximum patients 40 (40%) were treated with Cefo-Sulb, f/b 27 (27%) patient were treated with Meropenem, f/b 10 (10%) were treated with Pip-taz, f/b 8 (8%) patient were treated with Imipenem f/b 7 (7%) patient treated with Cephalexin, f/b 4 (4%) patient were treated with Levofloxacin, f/b 2 (2%) patient each were treated with Ceftriaxone and Fluconazole to treat Urosepsis till discharge.

It was also observed in our study that fungal infection with *Candida* was the most lethal organism causing death i.e. 66.67%, next lethal was *Pseudomonas* 62.5%, *Enterobacter* had 50% mortality and *E. coli* had least mortality of 19.23%, thus though being most common *E. coli* is least lethal whereas less common organism are more lethal. Thus there was statistically very highly significant **(p<0.05)** association of organism causing urosepsis and leading to mortality.

Discussion

The present study is an observational study of total 100 patients conducted in department of General Medicine in a tertiary care institute. In present study 23% blood culture were sterile and rest blood culture were, *E. coli* 38%, 8% had colonies of Proteus, 7% show Pseudomonas, Klebsiella and Polymicrobial colonies each. CONS was isolated in 4% patients, while Staphylococci and Streptococci growth was observed in 2% each, 1% patient's blood culture shown growth of *Enterobacter* and *Candida* each.

Degoricija V, et al. (2006)[18] also found positive blood culture rate at admission only 49% and found 31.2% E.coli followed by 9.6% Pseudomonas aeruginosa. This finding was also supported by Sugimoto K, et al. (2013)[19] and Buonaiuto VA, et al. (2014)[20] showing E.coli as the commonest organism in blood cultures with 18% and 67% respectively. Thus in all studies *E. Coli* was the most common organism causing urosepsis.

Out of total 100 patients urine culture, maximum growth of 52% of E. coli was seen, 11% had growth of *Proteus*, while *Klebsiella* and *Pseudomonas* growth was observed in 10% and 8% patients respectively. 5% patient's urine culture had growth of CONS, other organism *Acinetobacter*, *Candida*, *Enterobacter* growth in urine culture was seen in 3% study subjects each. 3% patients had sterile urine culture report, while polymicrobial growth was seen in 2% patients. Our result were consistent with Sugimoto K, et al. (2013),[19] Dreger NM, et al. (2015),[12] also found *E.coli* most common organism for urosepsis. Tandogdu Z, et al. (2013)[14] also reported *E.coli* 52% common and 2nd common was *Klebsiella* 11% in Asian study of bacterial spectrum in urosepsis.

In our study out of total 100 CKD patients empirically maximum patients 64 (64%) were treated with Cefoperazone-Sulbactum, followed by 18 (18%) patient were treated with meropenem, followed by 14 (14%) were treated with cephalexin other less common antibiotics used were Imipeneme, Piperacillin-Tazobactum, Cefo-Sulb with fluconazole, and Cefo-Sulb with Voriconazole to treat Urosepsis till discharge. In our study out of total 100 CKD patients, according to culture and sensitivity, maximum patients 40 (40%) were sensitive to Cefo-Sulb, followed by 27 (27%) patient were sensitive to meropenem in treating urosepsis. Dreger NM, et al. (2015),[12] also found similar results to this study.

Supportive therapy- 54 (54%) patient required IVF with Inotropic support for management of urosepsis, 17 (17%) patient required hemodialysis, (32%) patient required ventilatory support for treatment, similar result were found in research by Van Vught LA, et al. (2016)[21]. where ventilator was required in 37 % patients and inotropes in 22% patients. 35 (35%) were referred for urological intervention for treatment of urosepsis.

In the present study, 27 patients expired during the treatment in hospital due to urosepsis, mortality was higher in older age group, and male population had more mortality than female patients with a ratio of 2:1.

Conclusion

In present study, most common organism causing urosepsis was E. coli i.e. 52%. Most common empirical antibiotic given was Cefoperazone-Sulbactum (64%) and Meropenem (18%), while 40% patients were sensitive to Cefoperazone-Sulbactum and 27% patients to Meropenem. We suggest that, timely microbiological investigations including culture sensitivity helps in administering the proper antibiotics to the patient therby decreasing resistance and the chances of mortality.

References

1. HARRISON'S Principles of Internal Medicine, 19th edition, chapter 335, page 1811.

2. Todi S, Chatterjee S, Bhattacharyya M. Epidemiology of severe sepsis in India. Critical care. 2007 Mar;11(2):P65.
3. Mohan A, Shrestha P, Guleria R, Pandey RM, Wig N. Development of a mortality prediction formula due to sepsis/severe sepsis in a medical intensive care unit. Lung India: official organ of Indian Chest Society. 2015 Jul;32(4):313.
4. Brunkhorst FM. Epidemiology, economy and practice--results of the German study on prevalence by the competence network sepsis (SepNet). Anasthesiologie, Intensivmedizin, Notfallmedizin, Schmerztherapie: AINS. 2006 Jan;41(1):43-4.
5. Wagenlehner FM, Lichtenstern C, Rolfes C, Mayer K, Uhle F, Weidner W, Weigand MA. Diagnosis and management for urosepsis. International Journal of Urology. 2013 Oct;20(10):963-70.
6. Brun-Buisson C. The epidemiology of the systemic inflammatory response. Intensive care medicine. 2000 Feb 1;26(1):S064-74.
7. Johansen TE, Cek M, Naber K, Stratchounski L, Svendsen MV, Tenke P, PEP and PEAP study investigators, Board of the European Society of Infections in Urology. Prevalence of hospital-acquired urinary tract infections in urology departments. European urology. 2007 Apr 1;51(4):1100-12.
8. Bouza E, San Juan R, Munoz P, Voss A, Kluytmans J. A European perspective on nosocomial urinary tract infections II. Report on incidence, clinical characteristics and outcome (ESGNI-004 study). European Study Group on Nosocomial Infection. Clin Microbiol Infect 2001;**7**:532–42.
9. Hotchkiss RS, Karl IE. The pathophysiology and treatment of sepsis. New England Journal of Medicine. 2003 Jan 9;348(2):138-50.
10. Wagenlehner FM, Pilatz A, Naber KG, Weidner W. Therapeutic challenges of urosepsis. European Journal of Clinical Investigation. 2008 Oct;38:45-9.
11. Wagenlehner FM, Weidner W, Naber KG. Pharmacokinetic characteristics of antimicrobials and optimal treatment of urosepsis. Clinical pharmacokinetics. 2007 Apr 1;46(4):291-305.
12. Dreger NM, Degener S, Ahmad-Nejad P, Wöbker G, Roth S. Urosepsis—etiology, diagnosis, and treatment. Deutsches Ärzteblatt International. 2015 Dec;112(49):837.
13. Cek M, Tandoğdu Z, Wagenlehner F, Tenke P, Naber K, Bjerklund-Johansen TE. Healthcare-associated urinary tract infections in hospitalized urological patients—a global perspective: results from the GPIU studies 2003–2010. World journal of urology. 2014 Dec 1;32(6):1587-94.
14. Tandoğdu Z, Bartoletti R, Cai T, Çek M, Grabe M, Kulchavenya E, Köves B, Menon V, Naber K, Perepanova T, Tenke P. Antimicrobial resistance in urosepsis: outcomes from the multinational, multicenter global prevalence of infections in urology (GPIU) study 2003–2013. World journal of urology. 2016 Aug 1;34(8):1193-200.
15. Cardoso T, Ribeiro O, Costa-Pereira A, Carneiro A, A SACiUCI Study Group. Community-acquired and healthcare-related urosepsis: A multicenter prospective study. Critical Care. 2008 Mar 1;12(S2):P8.
16. Howell MD, Davis AM. Management of sepsis and septic shock. Jama. 2017 Feb 28;317(8):847-8
17. Dellinger RP, Levy MM, Rhodes A, Annane D, Gerlach H, Opal SM, Sevransky JE, Sprung CL, Douglas IS, Jaeschke R, Osborn TM. Surviving Sepsis Campaign: international guidelines for management of severe sepsis and septic shock, 2012. Intensive care medicine. 2013 Feb 1;39(2):165-228.
18. Degoricija V, Sharma M, Gradišer M, Šefer S, Vučičević Ž. Analysis of primary urosepsis in medical intensive care unit in University Hospital: intensive care unit survival and the effect of antimicrobial therapy. InOsmi simpozij o spolno prenosivim bolestima i urogenitalnim infekcijama, simpozij Slavka Schenwalda 2006 Jan 1.
19. Sugimoto K, Adomi S, Koike H, Esa A. Procalcitonin as an indicator of urosepsis. Research and reports in urology. 2013;5:77.
20. Buonaiuto VA, Marquez I, De Toro I, Joya C, Ruiz-Mesa JD, Seara R, Plata A, Sobrino B, Palop B, Colmenero JD. Clinical and epidemiological features and prognosis of complicated pyelonephritis: a prospective observational single hospital-based study. BMC infectious diseases. 2014 Dec;14(1):639.
21. van Vught LA, Klouwenberg PM, Spitoni C, Scicluna BP, Wiewel MA, Horn J, Schultz MJ, Nürnberg P, Bonten MJ, Cremer OL, van der Poll T. Incidence, risk factors, and attributable mortality of secondary infections in the intensive care unit after admission for sepsis. Jama. 2016 Apr 12;315(14):1469-79.

Conflict of Interest: Nil Source of support: Nil