Journal of Advanced Medical and Dental Sciences Research

@Society of Scientific Research and Studies

Journal home page:www.jamdsr.com doi:10.21276/jamdsr Index Copernicus value [ICV] =82.06

(e) ISSN Online: 2321-9599; (p) ISSN Print: 2348-6805

Original Research

To investigate the microbial composition of urosepsis in patients with chronic kidney disease (CKD) and evaluate its therapeutic management

[1]Sonia Bansal, [2]Ashok Kumar Agarwal

[1]Assistant Professor, Department of Micro-Biology, Gauri Devi Institute of Medical Science, India;
[2]Assistant Professor, Department of General Medicine, Gauri Devi Institute of Medical Science, India

ABSTRACT:
Aim: To investigate the microbial composition of urosepsis in patients with chronic kidney disease (CKD) and evaluate its therapeutic management. **Material and Methods:** Total 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 criteria for Chronic Kidney Disease (CKD). 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. **Results:** The findings of blood and urine cultures along with treatment given is enlisted in the tables below, On blood culture, most common pathogen isolated was *E. coli* i.e. 35%, 24% cultures were sterile, 10% had colonies of *Proteus*, 6% shown *Pseudomonas*, *Klebsiella* and Polymicrobial colonies each. CONS was isolated in 5% patients, while staphylococci and *Streptococci* growth was observed in 3% each, 1% patient's blood culture shown growth of *Enterobacter* and *Candida* each. Out of total 100 patients urine culture maximum growth of 49% of E. coli was seen, 12% had growth of Proteus, while Klebsiella and Pseudomonas growth was observed in 10% and 7% patients respectively. 60 (60%) were treated with Cefo-Sulb, f/b 19 (19%) patient were treated with Meropenem, f/b 15 (15%) were treated with Cephalexin f/b 2 (2%) each were treated with Imipeneme, Pip-Taz, Cefo-sulb with fluconazole, and Cefo-Sulb with Voriconazole to treat urosepsis till discharge. **Conclusion:** The predominant bacterium responsible for urosepsis in the current investigation was Escherichia coli, accounting for 49% of cases. The most often administered empirical antibiotics were Cefoperazone-Sulbactam (60%) and Meropenem (19%). Among the patients, 37% showed sensitivity to Cefoperazone-Sulbactam and 28% showed sensitivity to Meropenem.
Keywords: E.coli, urosepsis, CKD, Antibiotics

Received: 16-11- 2018 Accepted: 19-12-2018

Corresponding Author: Ashok Kumar Agarwal, Assistant Professor, Department of General Medicine, Gauri Devi Institute of Medical Science, India

This article may be cited as: Bansal S, Agarwal AK. To investigate the microbial composition of urosepsis in patients with chronic kidney disease (CKD) and evaluate its therapeutic management. J Adv Med Dent Scie Res 2019;7(1):264-268.

INTRODUCTION

The growing burden of chronic kidney disease (CKD) is a serious public health concern in the twenty-first century. Patients with CKD experience increased morbidity and mortality compared with the non-CKD population, typically from cardiovascular disease. However, infections in people with CKD are a significant source of morbidity and mortality too. The incidence of the commonly seen infectious complications is approximately three times greater among CKD patients than in the general population[1]. CKD is a risk factor for developing urinary tract infections (UTIs) mostly due to metabolic abnormalities resulting in alterations in primary host defense mechanisms. UTI comprises heterogeneous conditions ranging from mild cystitis, easily treated with oral antibiotics, to life-threatening sepsis and multiple organ failure. Severe or life-threatening infections are usually present as complicated UTI cases. The term complicated urinary tract infection is widely used for an infection that occurs in a patient wi th a structural or functional abnormality of the genitourinary tract that impedes urine flow or in the presence of the underlying diseases[2]. Therefore, all UTIs in patients with CKD are considered complicated. Urosepsis refers to a clinically manifested severe infection of the urinary tract. It is assumed that ascending UTI from the

bladder to the kidney, with resultant bacteremia, is the primary cause of urosepsis. Urosepsis in adults comprises approximately 25% of all sepsis cases following an episode of cUTI[3]. Gram-negative rods (75–85%) are most commonly associated with the above-mentioned condition, while gram-positive organisms are less frequently (15%) involved. While urosepsis patients have the lowest mortality rate among patients suffering from all causes of sepsis, urosepsis may still lead to mortality rates of 25% to 60% in different patient groups[4]. However, not all patients with cUTI will develop urosepsis. A number of studies have analyzed the risk factors for sepsis in different patients population but not in CKD patients with UTI[5-15]. Dellinger RP, et al. and Howell MD, et al. 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.

MATERIAL AND METHODS

This study was done in our institute. Total 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 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 25.0 (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, On blood culture, most common pathogen isolated was *E. coli* i.e. 35%, 24% cultures were sterile, 10% had colonies of *Proteus*, 6% shown *Pseudomonas*, *Klebsiella* and Polymicrobial colonies each. CONS was isolated in 5% patients, while staphylococci and *Streptococci* growth was observed in 3% each, 1% patient's blood culture shown growth of *Enterobacter* and *Candida* each.

Table 1: Organisms isolated on blood culture in study subjects

Organism	Frequency	Percent (%)
E. coli	35	35
Sterile	24	24
Proteus	10	10
Klebsiella	6	6
Polymicrobial	6	6
Pseudomonas	6	6
CONS	5	5
Staphylococci	3	3
Streptococci	3	3
Candida	1	1
Enterobacter	1	1
Total	100	100

Table 2 shows organisms isolated on urine culture. Out of total 100 patients urine culture maximum growth of 49% of E. coli was seen, 12% had growth of Proteus, while Klebsiella and Pseudomonas growth was observed in 10% and 7% patients respectively. 6% patient's urine culture had growth of CONS, other organism. Acinetobacter, Candida, Enterobacter growth in urine culture was seen in 4% study subjects each. 2% patients had sterile urine culture report, while Polymicrobial growth was seen in 2% patients.

Table 2: Organisms isolated on urine culture in study subjects

Organism	Frequency	Percent (%)
E. coli	49	49
Proteus	12	12
Klebsiella	10	10
Pseudomonas	7	7
CONS	6	6
Acinetobacter	4	4
Candida	4	4
Enterobacter	4	4
Sterile	2	2
Polymicrobial	2	2
Total	100	100

Table 3: Empirical antibiotic administered to study subjects.

Antibiotic	Frequency	Percent (%)
Cefo-Sulb	60	60
Meropeneme	19	19
Cephalexin	15	15
Cefo-Sulb + Fluconazole	2	2
Cefo-Sulb + Voriconazole	2	2
Imipeneme	1	1
Pip-Taz	1	1
Total	100	100

Table 3 shows Empirical antibiotic administered to study subjects. In our study out of total 100 CKD patients, in empirical treatment maximum patients 60 (60%) were treated with Cefo-Sulb, f/b 19 (19%) patient were treated with Meropenem, f/b 15 (15%) were treated with Cephalexin f/b 2 (2%) each were treated with Imipeneme, Pip-Taz, Cefo-sulb with fluconazole, and Cefo-Sulb with Voriconazole to treat urosepsis till discharge.

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

Antibiotic	Frequency	Percent (%)
Cefo-Sulb	37	37
Meropenem	28	28
Pip-Taz	11	11
Imipenem	9	9
Cephalexin	8	8
Levofloxacin	5	5
Ceftriaxone	1	1
Fluconazole	1	1
Total	100	100

Table 4 shows Antibiotic sensitive to organism administered to study subjects. In our study out of total 100 CKD patients, according to culture and sensitivity, maximum patients 37 (37%) were treated with Cefo-Sulb, f/b 28 (28%) patient were treated with Meropenem, f/b 11 (11%) were treated with Pip-taz, f/b 9 (9%) patient were treated with Imipenem f/b 8 (8%) patient treated with Cephalexin, f/b 5 (5%) patient were treated with Levofloxacin, f/b 1 (1%) 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%, next lethal was *Pseudomonas* 62%, *Enterobacter* had 49% mortality and *E. coli* had least mortality of 20%, 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 in a tertiary care institute. In present study on blood culture, most common pathogen isolated was *E. coli* i.e. 35%, 24% cultures were sterile, 10% had colonies of *Proteus*, 6% shown *Pseudomonas*, *Klebsiella* and Polymicrobial colonies

each. CONS was isolated in 5% patients, while staphylococci and *Streptococci* growth was observed in 3% each, 1% patient's blood culture shown growth of *Enterobacter* and *Candida* each. Degoricija V, et al[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.[19] and Buonaiuto VA, et al.[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 49% of E. coli was seen, 12% had growth of Proteus, while Klebsiella and Pseudomonas growth was observed in 10% and 7% patients respectively. 6% patient's urine culture had growth of CONS, other organism. Acinetobacter, Candida, Enterobacter growth in urine culture was seen in 4% study subjects each. 2% patients had sterile urine culture report, while Polymicrobial growth was seen in 2% patients. Our result were consistent with Sugimoto K, et al.,[19] Dreger NM, et al.,[12] also found *E.coli* most common organism for urosepsis. Tandogdu Z, et al.[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, in empirical treatment maximum patients 60 (60%) were treated with Cefo-Sulb, f/b 19 (19%) patient were treated with Meropenem, f/b 15 (15%) were treated with Cephalexin f/b 2 (2%) each were treated with Imipeneme, Pip-Taz, Cefo-sulb with fluconazole, and Cefo-Sulb with Voriconazole to treat urosepsis till discharge. out of total 100 CKD patients, according to culture and sensitivity, maximum patients 37 (37%) were treated with Cefo-Sulb, f/b 28 (28%) patient were treated with Meropenem, f/b 11 (11%) were treated with Pip-taz, f/b 9 (9%) patient were treated with Imipenem f/b 8 (8%) patient treated with Cephalexin, f/b 5 (5%) patient were treated with Levofloxacin, f/b 1 (1%) patient each were treated with Ceftriaxone and Fluconazole to treat Urosepsis till discharge. Dreger NM, et al.,[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.[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, 25 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

The predominant bacterium responsible for urosepsis in the current investigation was Escherichia coli, accounting for 49% of cases. The most often administered empirical antibiotics were Cefoperazone-Sulbactam (60%) and Meropenem (19%). Among the patients, 37% showed sensitivity to Cefoperazone-Sulbactam and 28% showed sensitivity to Meropenem. Timely microbiological studies, such as culture sensitivity testing, are recommended to facilitate the administration of appropriate antibiotics to patients. This approach helps to reduce antibiotic resistance and the risk of death.

REFERENCES

1. Naqvi SB, Collins AJ. Infectious complications in chronic kidney disease. Adv Chronic Kidney Dis. 2006;13(3):199-204. doi: 10.1053/j.ackd.2006.04.004, PMID 16815225.
2. Lichtenberger P, Hooton TM. Complicated urinary tract infections. Curr Infect Dis Rep. 2008;10(6):499-504. doi: 10.1007/s11908-008-0081-0, PMID 18945392.
3. Wagenlehner FM, Lichtenstern C, Rolfes C, Mayer K, Uhle F, Weidner W, et al. Diagnosis and management for urosepsis. Int J Urol. 2013;20(10):963-70. doi: 10.1111/iju.12200, PMID 23714209.
4. Wagenlehner FME, Pilatz A, Naber KG, Weidner W. Therapeutic challenges of urosepsis. Eur J Clin Investig. 2008;38;Suppl 2:45-9. doi: 10.1111/j.1365-2362.2008.02008.x, PMID 18826481.
5. Peach BC, Garvan GJ, Garvan CS, Cimiotti JP. Risk factors for urosepsis in older adults: a systematic review. Gerontol Geriatr Med. 2016;2:2333721416638980. doi: 10.1177/2333721416638980, PMID 28138493.
6. Rowe TA, Juthani-Mehta M. Urinary tract infection in older adults. Aging Health. 2013;9(5):519-28. doi: 10.2217/ahe.13.38, PMID 24391677.
7. Hakeem LM, Bhattacharyya DN, Lafong C, Janjua KS, Serhan JT, Campbell IW. Diversity and complexity of urinary tract infection in diabetes mellitus. Diabetes & Vascular Disease. 2009;9(3):119-25. doi: 10.1177/1474651409105654.
8. Wagenlehner FME, Tandogdu Z, Bjerklund Johansen TE. An update on classification and management of urosepsis. Curr Opin Urol. 2017;27(2):133-7. doi: 10.1097/MOU.0000000000000364, PMID 27846034.
9. Qiang XH, Yu TO, Li YN, Zhou LX. Prognosis risk of urosepsis in critical care medicine: a prospective observational study. BioMed Res Int. 2016;2016:9028924. doi: 10.1155/2016/9028924, PMID 26955639.
10. Abou Dagher G, Harmouche E, Jabbour E, Bachir R, Zebian D, Bou Chebl RB. Sepsis in hemodialysis patients. BMC Emerg Med. 2015;15:30. doi: 10.1186/s12873-015-0057-y, PMID 26467100.
11. Wagenlehner FM, Weidner W, Naber KG. Pharmacokinetic characteristics of antimicrobials and optimal treatment of urosepsis. Clin Pharmacokinet. 2007 Apr 1;46(4):291-305. doi: 10.2165/00003088-200746040-00003, PMID 17375981.
12. Dreger NM, Degener S, Ahmad-Nejad P, Wöbker G, Roth S. Urosepsis—etiology, diagnosis, and treatment. Dtsch Ärztebl Int. 2015 Dec;112(49):837-47; quiz 848.

doi: 10.3238/arztebl.2015.0837, PMID 26754121.
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 J Urol. 2014 Dec 1;32(6):1587-94. doi: 10.1007/s00345-013-1218-9, PMID 24452449.
14. Tandoğdu Z, Bartoletti R, Cai T, Çek M, Grabe M, Kulchavenya E et al. Antimicrobial resistance in urosepsis: outcomes from the multinational, multicenter global prevalence of infections in urology (GPIU) study 2003-2013. World J Urol. 2016 Aug 1;34(8):1193-200. doi: 10.1007/s00345-015-1722-1, PMID 26658886.
15. Cardoso T, Ribeiro O, Costa-Pereira A, Carneiro A. A SACiUCI study group. Community-acquired and healthcare- related urosepsis: A multicenter prospective study. Crit Care. 2008 Mar 1;12;Suppl 2:8. doi: 10.1186/cc6229.
16. Howell MD, Davis AM. Management of sepsis and septic shock. JAMA. 2017 Feb 28;317(8):847-8. doi: 10.1001/jama.2017.0131, PMID 28114603.
17. Dellinger RP, Levy MM, Rhodes A, Annane D, Gerlach H, Opal SM et al. Surviving Sepsis Campaign: international guidelines for management of severe sepsis and septic shock, 2012. Intensive Care Med. 2013 Feb 1;39(2):165-228. doi: 10.1007/s00134-012-2769-8, PMID 23361625.
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. In: Osmi 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. Res Rep Urol. 2013;5:77-80. doi: 10.2147/RRU.S42711, PMID 24400237.
20. Buonaiuto VA, Marquez I, De Toro I, Joya C, Ruiz-Mesa JD, Seara R et al. Clinical and epidemiological features and prognosis of complicated pyelonephritis: a prospective observational single hospital-based study. BMC Infect Dis. 2014 Dec;14(1):639. doi: 10.1186/s12879-014-0639-4, PMID 25492862.
21. van Vught LA, Klein Klouwenberg PM, Spitoni C, Scicluna BP, Wiewel MA, Horn J et al. 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. doi: 10.1001/jama.2016.2691, PMID 26975785.