

Microbiological profile and antibiotic sensitivity pattern of bacteria isolated from patients with chronic bacterial prostatitis

Microbiological profile of chronic bacterial prostatitis

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Abstract

Chronic bacterial prostatitis is a persistent infection of the prostate characterized by frequent relapses due to incomplete eradication of the causative organisms, with a negative impact on patient's quality of life. This study aimed to determine the most common bacterial causative agents and their antibiotic sensitivity patterns in patients with chronic bacterial prostatitis in Duhok, Kurdistan, northern Iraq. A standard Meares-Stamey four-glass test was performed for all males presenting with chronic prostatitis symptoms for more than 3 months. Men with high leukocyte counts and bacterial growth in expressed prostatic secretion (EPS) and post-prostate massage urine (VB3) samples but negative first-voided (VB1) and midstream urine (VB2) samples were included in the study. The Phoenix system (Becton Dickinson) was used for bacterial identification and antimicrobial susceptibility testing. Staphylococcus spp. were the most prevalent microorganisms in patients with chronic prostatitis (60.8%), followed by Escherichia coli and Enterococcus spp. (13.7%). Most patients with chronic prostatitis who were diagnosed with Staphylococcus spp. exhibited high resistance to benzylpenicillin (75.0%), oxacillin (60.5%), and ampicillin (59.0%). Patients diagnosed with Enterococcus spp. showed high resistance to quinupristin-dalfopristin (20.0%), cefoxitin screen (15.7%), clindamycin (16.9%), tetracycline (16.9%), and rifampicin (17.1%). Among those diagnosed with Streptococcus spp., most had resistance to oxacillin (7.4%), tobramycin (8.0%), erythromycin (8.4%), clindamycin (8.4%), tetracycline (8.4%), and mupirocin (12.1%). The patients with E. coli had resistance to extended-spectrum β -lactamases (ESBL) (45.5%) and cefepime (25.0%). In summary, we found that the most prevalent pathogens from patients with chronic bacterial prostatitis are E. coli, Enterococcus spp., and Staphylococcus aureus. Gram-positive isolates showed the highest resistance to benzylpenicillin, fosfomycin, ampicillin, tetracycline, rifampicin, and mupirocin. Moreover, gram-negative bacteria were most resistant to ESBL, cefepime, and ampicillin-sulbactam. To manage this condition, physicians should take into consideration the development of multi-drug resistance among the pathogenic agents.

Keywords

Chronic; Bacterial; prostatitis; Duhok; Kurdistan

Introduction

Chronic prostatitis (CP)/chronic pelvic pain syndrome (CPPS) is a common urological problem and is suggested to be the most common reason for urology clinic visits among adult men before age 50 and the third most common cause among those older than 50 years of age [1, 2]. CP causes a wide array of symptoms, including lower urinary tract symptoms (irritative and obstructive) and pain in the perineum, scrotum, lower abdomen, and back; in addition, it affects sexual function and usually has a tremendous negative impact on the quality of life of patients [2]. The NIH has classified prostatitis into four categories; among these, category II represents chronic bacterial prostatitis (CBP) [1, 3], which is characterized by CP symptoms associated with active bacterial infection. Such infections can be diagnosed via the Meares-Stamey four-glass test, in which first-voided urine (VB1), midstream urine (VB2), expressed prostatic secretions (EPS), and post-prostate massage urine (VB3) are collected and examined for leukocyte counts and bacterial growth [1]. CBP is diagnosed by identifying higher leukocyte counts and bacterial growth in EPS and VB3 than those identified in VB1 and VB2 [1]. CBP is commonly caused by *Escherichia coli* and other gram-negative *Enterobacteriaceae*, occasionally by *Pseudomonas* species, and, rarely, by gram-positive enterococci. It is currently thought that atypical microorganisms such as *Chlamydia trachomatis*, *Ureaplasma urealyticum*, and *Mycoplasma hominis* can be implicated in some cases of CP; however, these species are difficult to culture and identify under standard conditions [4].

Although constituting only about 20% of CP/CPPS cases, CBP is the only potentially curable type if proper antibiotic therapy is administered, usually in prolonged courses; however, it is commonly characterized by frequent relapses [2]. CBP antibiotic treatment is complicated by the poor capability of antibiotics to penetrate prostatic tissue, rising rates of antibiotic resistance, and the need for prolonged courses. Therefore, it is necessary to correctly identify the causative organisms and the most appropriate drug therapy in order to achieve optimal results and avoid the side effects of drugs. Considering the diversity of infection-causing microorganisms and the high resistance patterns of such microorganisms in our Kurdistan Region of Iraq [5-9], the purpose of this study was to identify the most common causative organisms in patients with CBP in the Duhok area and to identify their antibiotic sensitivity patterns.

Materials and methods

Sample collection

After conducting an examination, carefully obtaining the patient history, and receiving patient consent, a classical four-glass test was performed for all patients. First, the patient was asked to collect the first voided urine stream sample and midstream urine sample in containers labelled VB1 and VB2, respectively. Subsequently, prostatic massage was performed for patients in the outpatient clinic, and if there was urethral secretion, it was collected in the "EPS" container. Then, patients were asked to collect a urine sample in the "VB3" container. The samples were then sent to the laboratory for microscopic examination and bacterial culture.

Inclusion criteria

All males presenting to the urology outpatient clinic with symptoms suggesting CP/CPPS for more than 3 months, who were 18 years or older and agreed to participate, were included in the study. Patients with bacterial growth and pyuria in VB1 and VB2 were diagnosed as having urethritis or cystitis, treated according to culture and sensitivity, and excluded from the study population.

Patients with negative VB1 and VB2 samples and either only pyuria (>10 leukocytes per high-power field [HPF] on microscopic examination) in either or both EPS and VB3 but no bacterial growth were diagnosed with abacterial prostatitis, and those with negative EPS and VB3 samples for leukocytes and bacterial growth were diagnosed with CPPS; these patients were also excluded from the study population.

Only patients with negative VB1 and VB2 for leukocytes and bacteriuria and with pyuria (>10 leukocytes per HPF under microscopic examination) and significant bacterial growth in either or both EPS and VB3 were included in the study, and these samples were sent to determine antibiotic sensitivity.

Antimicrobial susceptibility test

The Phoenix system (Becton Dickinson, Franklin Lakes, NJ, USA) was used for bacterial identification and antimicrobial susceptibility testing. The test was performed according to the manufacturer's instructions.

Statistics

The prevalence rates of microorganisms, including *Staphylococcus* spp., *Enterococcus* spp., *Streptococcus* spp., *Acinetobacter* spp., *E. coli*, *Proteus* spp., *Morganella* spp., and *Klebsiella* spp. are presented in terms of frequency and percentage. In addition, the antimicrobial resistance patterns against gram-positive and gram-negative microbes in patients with CP were determined using descriptive statistics, including frequency and percentage. Statistical calculations were performed using the Statistical Package for Social Sciences 24 (SPSS 24; IBM Corp, Armonk, NY, USA).

Results

The results indicated that *Staphylococcus* spp. were the most prevalent microorganisms in patients with CP (60.8%), followed by *E. coli* and *Enterococcus* spp. (13.7%). Among *Staphylococcus* spp., *Staphylococcus haemolyticus* was the most prevalent (29.4%), followed by *Staphylococcus epidermidis* (11.8%). Among *Streptococcus* spp., *Streptococcus agalactiae* and *Streptococcus anginosus* were most prevalent (2.0%), as shown in Table 1.

In most patients with CP who were diagnosed with *Staphylococcus* spp., the pathogenic bacteria showed the highest resistance to benzylpenicillin (75.0%), oxacillin (60.5%), ampicillin (59.0%), erythromycin (57.8%), and fosfomicin (73.9%), mupirocin (75.8%), and high-level gentamicin

(63.8%). Among the patients who were diagnosed with *Enterococcus* spp., resistance was highest against quinupristin-dalfopristin (20.0%), ceftiofur (15.7%), clindamycin (16.9%), tetracycline (16.9%), and rifampicin (17.1%). Among those diagnosed with *Streptococcus* spp., most had resistance to oxacillin (7.4%), tobramycin (8.0%), erythromycin (8.4%), clindamycin (8.4%), tetracycline (8.4%), and mupirocin (12.1%), as presented in Table 2.

The results showed that patients with CP and *Acinetobacter* spp. were resistant to extended-spectrum β -lactamases (ESBL) (9.1%) and ceftazidime (6.3%). The patients with *E. coli* had resistance to ESBL (45.5%) and ceftazidime (25.0%). Additionally, patients with *Proteus* spp. were resistant to ESBL (9.1%), those with *Morganella morganii* were resistant to ESBL (9.1%), and those with *Klebsiella* spp. were resistant to ampicillin-sulbactam (9.1%), ceftazidime (6.3%), and ceftazidime (6.3%), as presented in Table 3.

Discussion

Prostatitis is one of the most common urological conditions, and many urologists find it difficult to treat this disease efficiently. It is estimated that up to half of men suffer from symptoms of prostatitis during their lifetime [10]. Urinary tract infections are a major complication in patients with prostatitis, which commonly affects elderly males worldwide [11]. Despite recent progress in the treatment of CBP, many cases result in relapse. Increased antibiotic resistance patterns of the bacteria responsible for CBP, particularly in Iraq, have been proposed as one of the most likely causative factors [12, 13]. There are a limited number of studies addressing this subject in the Kurdistan Region of Iraq. Therefore, we aimed to study the antibiotic sensitivity pattern of responsible bacteria isolated from patients with CBP.

This study demonstrated that *Staphylococcus* spp. were the most common bacterial causes in patients with CBP (60.8%), followed by *E. coli* and *Enterococcus* spp. (13.7%). In contrast, previous studies reported that representative *Enterobacteriaceae* and *Corynebacterium* spp. were the most common pathogens isolated in patients with CBP, including *E. coli* (44%), *Corynebacterium* spp. (44.8%), and *Enterococcus* spp. (40.8%) [14]. Another study also found that *Enterobacteriaceae*, particularly *E. coli*, are the predominant pathogens in bacterial prostatitis (acute and chronic); however, other uropathogens are also found to a lesser extent, such as *Pseudomonas aeruginosa* [15]. Differences in the frequency of many pathogens between the present study and other studies might represent time trends in prostatic bacterial colonization [16]. To confirm the above, gram-positive bacteria were more frequently identified in the current study than previously [16]. This epidemiological shift to gram-positive bacteria could be ascribed to the globally increasing bacterial resistance to most antibiotics [17].

Concerning the antimicrobial susceptibility test, it should be noted that significant changes in bacterial susceptibility patterns have been established over the last two decades [18]. In agreement with other studies in the region [19-21], our findings indicated that the majority of patients with CP who were diagnosed with *Staphylococcus* spp. were highly resistant to

benzylpenicillin, oxacillin, ampicillin, erythromycin, fosfomycin, mupirocin, and high-level gentamicin. Most prostatitis patients diagnosed with *Enterococcus* spp. revealed high resistance to quinupristin-dalfopristin. The observed increase in quinupristin resistance among *Enterococcus* spp. that cause CPB can be attributed to the wide use of quinipristinin clinical practice. Additionally, it was observed that the isolates of *Streptococcus* spp. had relatively high resistance to tobramycin, erythromycin, clindamycin, tetracycline, and mupirocin. The high resistance to most tested antibacterial agents shown by the *Streptococcus* spp. could be due to the fact that patients with CBP experience recurrent urinary tract infections, which likely led to the use of different antibiotics, hence the development of resistant strains.

The results also showed that patients with CP who had *Acinetobacter* spp. were resistant to ESBL and cefazolin. Furthermore, *E. coli* and *Proteus* isolates in patients with CP showed decreased susceptibility to ESBL and cefepime. In addition, *Klebsiella* spp. isolates from patients were resistant to ampicillin-sulbactam, cefazolin, and cefepime. Therefore, treatment should be tailored to the antibiotic susceptibility test results. These findings are in agreement with those of other previous studies [22], which found multi-drug resistance in *E.coli*, *Klebsiella* spp., and *P.aeruginosa*.

Conclusion

In this study, we found that the most prevalent pathogens from patients with CBP are *E. coli*, *Enterococcus* spp., and *S. aureus*. Gram-positive isolates showed the highest resistance to benzylpenicillin, fosfomycin, ampicillin, tetracycline, rifampicin, and mupirocin. Meanwhile, gram-negative bacteria exhibited the highest resistance to ESBL, cefepime, and ampicillin-sulbactam. Therefore, to manage CBP, physicians should take into consideration the development of multi-drug resistance among the pathogenic agents.

References

1. Murphy AB, Macejko A, Taylor A, Nadler RB. Chronic Prostatitis. *Drugs* 2009;69(1):71-84.
2. McNaughton Collins M, Pontari MA, O'Leary MP, Calhoun EA, Santanna J, Landis JR, Kusek JW, Litwin MS, Network atCPCR. Quality of Life Is Impaired in Men with Chronic Prostatitis the Chronic Prostatitis Collaborative Research Network*. *Journal of General Internal Medicine* 2001;16(10):656-662.
3. Krieger JN, Nyberg J, Leroy, Nickel JC. NIH Consensus Definition and Classification of Prostatitis. *JAMA* 1999;282(3):236-237.
4. Lipsky BA, Byren I, Hoey CT. Treatment of Bacterial Prostatitis. *Clinical Infectious Diseases* 2010;50(12):1641-1652.

5. Naqid IA, Hussein NR, Balatay A, Saeed KA, Ahmed HA. Antibiotic Susceptibility Patterns of Uropathogens Isolated from Female Patients with Urinary Tract Infection in Duhok Province, Iraq. *Jundishapur Journal of Health Sciences* 2020;12(3).
6. Naqid IA, Balatay AA, Hussein NR, Ahmed HA, Saeed KA, Abdi SA. Bacterial Strains and Antimicrobial Susceptibility Patterns in Male Urinary Tract Infections in Duhok Province, Iraq. *Middle East Journal of Rehabilitation and Health Studies* 2020;7(3):e103529.
7. Naqid IA, Balatay AA, Hussein NR, Saeed KA, Ahmed HA, Yousif SH. Antibiotic Susceptibility Pattern of Escherichia coli Isolated from Various Clinical Samples in Duhok City, Kurdistan Region of Iraq. *International Journal of Infection* 2020;7(3).
8. Naqid IA, Hussein NR, Balatay AA, Abdullah K. The Antimicrobial Resistance Pattern of Klebsiella pneumonia Isolated from the Clinical Specimens in Duhok City in Kurdistan Region of Iraq. 2020.
9. Hussein NR, Daniel S, Salim K, Assafi MS. Urinary tract infections and antibiotic sensitivity patterns among women referred to Azadi teaching hospital, Duhok, Iraq. *Avicenna Journal of Clinical Microbiology and Infection* 2017;5(2):27-30.
10. Hung SC, Lai SW, Tsai PY, Chen PC, Wu HC, Lin WH, Sung FC. Synergistic interaction of benign prostatic hyperplasia and prostatitis on prostate cancer risk. *Br J Cancer* 2013;108(9):1778-1783.
11. Silverio F, Gentile V, Pastore A, Voria G, Mariotti G, Sciarra A. Benign Prostatic Hyperplasia: What About a Campaign for Prevention? *Urologia internationalis* 2004;72:179-188.
12. Abdulkareem WL, Hussein NR, Mohammed AA, Arif SH, Naqid IA. Risk Factors Association for MRSA Nasal Colonization in Preoperative Patients in Azadi Teaching Hospital- Duhok, Kurdistan Region, Iraq. *Science Journal of University of Zakho* 2020;8(3):88-91.
13. Assafi MS, Ibrahim NM, Hussein NR, Taha AA, Balatay AA. Urinary bacterial profile and antibiotic susceptibility pattern among patients with urinary tract infection in duhok city, kurdistan region, Iraq. *International Journal of Pure and Applied Sciences and Technology* 2015;30(2):54.
14. Dv K, Va C, Salam N, Gok A, editors. Pattern of Bacterial Isolates and Antimicrobial Susceptibility of Urine Culture in Men with Chronic Bacterial Prostatitis and Levels PSA Before and After Treatment Patient; 2017.
15. Oshodi A, Nwabuisi C, Ii A, Fadeyi A, Oshodi A, Nwabuisi C, Popoola A, Edungbola L, Agbede O, Ii A, Fadeyi A, Raheem R. Bacterial Uropathogen among Benign Prostatic Hyperplasia Patients at a Tertiary Hospital in Nigeria. *Open Journal of Medical Microbiology* 2015;5:22-27.

16. Mazzoli S. Conventional bacteriology in prostatitis patients: microbiological bias, problems and epidemiology on 1686 microbial isolates. *Archivio italiano di urologia, andrologia : organo ufficiale [di] Societa italiana di ecografia urologica e nefrologica* 2007;79(2):71-75.
17. Wagenlehner FME, Weidner W, Pilatz A, Naber KG. Urinary tract infections and bacterial prostatitis in men. *Current Opinion in Infectious Diseases* 2014;27(1).
18. Kahlmeter G. An international survey of the antimicrobial susceptibility of pathogens from uncomplicated urinary tract infections: the ECO.SENS Project. *J Antimicrob Chemother* 2003;51(1):69-76.
19. Rasheed N, Hussein NR. The Nasal Carriage of Staphylococcus aureus and Its Antimicrobial Susceptibility Pattern in Secondary School Students in Kurdistan Region, Iraq. *Journal of Kermanshah University of Medical Sciences* 2020;24(1):e99490.
20. Mohammed AA, Hussein NR, Arif SH, Daniel S. Surgical site infection among patients with Staphylococcus aureus nasal carriage. *International Journal of Surgery Open* 2020.
21. Hussein N, Salih RS, Rasheed NA. Prevalence of Methicillin-Resistant Staphylococcus aureus in Hospitals and Community in Duhok, Kurdistan Region of Iraq. *International Journal of Infection* 2019;6(2):e89636.
22. Mishra PP, Prakash V, Singh K, Mog H, Agarwal S. Bacteriological Profile of Isolates From Urine Samples in Patients of Benign Prostatic Hyperplasia and or Prostatitis Showing Lower Urinary Tract Symptoms. *Journal of clinical and diagnostic research : JCDR* 2016;10(10):Dc16-dc18.

Table 1. Frequency of microorganisms in children with chronic prostatitis

Microorganism	Microbes (n=102)	Frequency	Percent
Staphylococcus Spp.	Staphylococcus aureus	2	2.0
	Staphylococcus hominis	5	4.9
	Staphylococcus epidermidis	12	11.8
	Staphylococcus	30	29.4
	haemolyticus	10	9.8
	Staphylococcus lentus	2	2.0
	Staphylococcus warreni	1	1.0
	Staphylococcus captis		
Subtotal	Staphylococcus Spp.	62	60.8
Enterococcus Spp.	Enterococcus faecalis	14	13.7
Streptococcus Spp.	Streptococcus agalactiate	2	2.0

	Streptococcus anginosus	2	2.0
	Streptococcus thoraltensis	1	1.0
	Streptococcus galloctyticus	1	1.0
	Streptococcus salivarius	1	1.0
Subtotal	Streptococcus Spp.	7	6.9
Acinetobacter Spp.	Acinetobacter baumannii	1	1.0
E. Coli Spp.	Escherichia coli	14	13.7
Proteus Spp.	Proteus mirabilis	1	1.0
Morganella Spp.	Morganellamorganii	1	1.0
Klebsiella Spp.	Klebsiella pneumoniae	2	2.0

Table 2: Antimicrobial resistance patterns among gram-positive bacteria in patients with chronic prostatitis

Antibiotic (n=102)	Organism/Number of Isolates (Percent of Resistance)		
	Staphylococcus Sp.	Enterococcus Sp.	Streptococcus Sp.
β-lactamase	0 (0.0)	0 (0.0)	4 (5.9)
Cefoxitin screen	14 (15.7)	14 (15.7)	6 (6.7)
Benzylpenicillin	60 (75.0)	11 (13.8)	5 (6.3)
Benzylpenicillin	60 (75.0)	11 (13.8)	5 (6.3)
Oxacillin	49 (60.5)	14 (17.3)	6 (7.4)
Ampicillin	36 (59.0)	2 (3.3)	0 (0.0)
Gentamicin	8 (7.9)	14 (13.9)	6 (5.9)
Tobramycin	5 (10.0)	4 (8.0)	4 (8.0)
Levofloxacin	13 (20.0)	3 (4.6)	4 (6.2)
Moxifloxacin	0 (0.0)	14 (17.1)	5 (6.1)
Inducible clindamycin	46 (55.4)	14 (16.9)	7 (8.4)
Erythromycin	48 (57.8)	7 (8.4)	7 (8.4)
Clindamycin	31 (37.3)	14 (16.9)	7 (8.4)

Linezolid	1 (1.2)	0 (0.0)	4 (4.9)
Teicoplanin	2 (3.0)	0 (0.0)	4 (6.0)
Vancomycin	13 (15.7)	2 (2.4)	4 (4.8)
Tetracycline	36 (43.4)	14 (16.9)	7 (8.4)
Tigecycline	0 (0.0)	0 (0.0)	4 (4.7)
Fosfomycin	51 (73.9)	11 (15.9)	5 (7.2)
Nitrofurantoin	0 (0.0)	0 (0.0)	5 (7.4)
Fusidicacid	50 (74.6)	11 (16.4)	5 (7.5)
Mupirocin	25 (75.8)	4 (12.1)	4 (12.1)
Rifampicin	7 (8.5)	14 (17.1)	6 (7.3)
Trimethoprim sulfamethoxazole	21 (20.6)	14 (13.7)	6 (5.9)
Imipenem	18 (34.6)	7 (13.5)	1 (1.9)
High-level gentamicin	30 (63.8)	8 (17.0)	4 (8.5)
High-level streptomycin	29 (61.7)	8 (17.0)	4 (8.5)
Ciprofloxacin	16 (23.9)	4 (6.0)	2 (3.0)
Quinupristin-dalfopristin	0 (0.0)	3 (20.0)	0 (0.0)
The bold numbers show the most resistant microorganisms.			

Table 3. Antimicrobial resistance patterns among gram-negative bacteria in patients with chronic prostatitis

Antibiotic (n=102)	Organism/Number of Isolates (Percent of Resistance)				
	Acinetobacter Sp.	E. coli	Proteus Sp.	Morganella morganii	Klebsiella Sp.
Cefoxitin screen		1 (1.1)			0 (0.0)
Ampicillin	1 (1.6)	11 (18.0)	1 (1.6)	1 (1.6)	2 (3.3)
Gentamicin	0 (0.0)	1 (1.0)	1 (1.0)	0 (0.0)	1 (1.0)
Tobramycin	1 (2.0)	2 (4.0)	0 (0.0)	0 (0.0)	0 (0.0)
Levofloxacin	0 (0.0)	3 (4.6)	0 (0.0)	0 (0.0)	0 (0.0)
Tigecycline		0 (0.0)			

Fosfomycin		1 (1.4)			1 (1.4)
Nitrofurantoin	1 (1.5)	0 (0.0)	1 (1.5)	1 (1.5)	0 (0.0)
Trimethoprim sulfamethoxazole	0 (0.0)	3 (2.9)	1 (1.0)	1 (1.0)	1 (1.0)
Imipenem	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Extended-spectrum β - lactamase	1 (9.1)	5 (45.5)	1 (9.1)	1 (9.1)	0 (0.0)
Ciprofloxacin	0 (0.0)	3 (4.5)	0 (0.0)	1 (1.5)	0 (0.0)
Ampicillin-sulbactam	0 (0.0)	3 (27.3)	0 (0.0)	1 (9.1)	1 (9.1)
Piperacillin tazaboctam	0 (0.0)	2 (10.5)	1 (5.3)	0 (0.0)	0 (0.0)
Cefazolin	1 (6.3)	4 (25.0)	1 (6.3)	1 (6.3)	1 (6.3)
Ceftazidime	0 (0.0)	2 (14.3)	1 (7.1)	0 (0.0)	1 (7.1)
Ceftriaxone	0 (0.0)	4 (21.1)	1 (5.3)	0 (0.0)	1 (5.3)
Cefepime	1 (6.3)	4 (25.0)	1 (6.3)	0 (0.0)	1 (6.3)
Ertapenem	1 (5.3)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Amoxicillin clavulanic acid	1 (5.3)	2 (10.5)	1 (5.3)	1 (5.3)	0 (0.0)