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Etiology and Antimicrobial Resistance Pattern of Sepsis and Urinary Tract Infections in HIV-Infected Patients from Southwestern Iran

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ABSTRACT

Backgrounds: Sepsis is a systemic inflammatory response syndrome triggered by an infectious agent and an important cause of admission to intensive care units (ICU), especially in immunodeficient patients. The aim of this study was to determine the spectrum of bacterial etiology and antibacterial susceptibility pattern of sepsis and urinary tract infections (UTIs) in Iranian HIV-infected patients.

Materials & Methods: This retrospective cross-sectional study was conducted on HIV/AIDS patients for a period of ten years from January 2005 to January 2015 at two major hospitals in southwestern Iran. Standard microbiological methods were used for the isolation and identification of bacteria from samples. Antimicrobial susceptibility tests were done using disk diffusion method.

Findings: Out of 228 samples collected, the frequency of culture-positive blood and urine samples was 23.2% (n = 53) and 9.6% (n=22), respectively. Among culture-positive blood samples, *Staphylococcus aureus* (N = 17, 32.1%) and *Pseudomonas* (N = 5, 9.4%) were the main etiologic agents. While among 22 culture-positive urine samples, the predominant bacteria were *Enterococci* (N = 7, 31.8%) and *Escherichia coli* (N = 5, 22.7%). Antibacterial susceptibility testing results showed that Gram-positive bacteria were mostly susceptible to vancomycin, rifampin, and co-trimoxazole; meanwhile, Gram-negative bacteria were mostly susceptible against tobramycin, amoxicillin/clavulanate, and aztreonam.

Conclusions: In summary, this study findings highlighted the emergence and spread of opportunistic infections and a high level of antibiotic resistance among HIV-infected patients; therefore, restricted infection control strategies must be pursued in these hospitals.

Keywords: Sepsis, Urinary tract infections, HIV/AIDS, Antibiotic resistance

CITATION LINKS

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Introduction

Bloodstream infection is a systemic inflammatory response syndrome trigered by an infectious agent and an important cause of admission to intensive care units (ICU) [1, 2]. In general, bloodstream infection due to serious complications including acute organ dysfunction and hemodynamic instability is responsible for a significant rate of mortality in ICU [3]. According to the latest UNAIDS reports, 78 million of population have become infected with human immunodeficiency virus (HIV), and 35 million have died from AIDS-related illnesses worldwide [4]. Although the exact number of HIV-positive adults and children in Iran is not clear, recent estimates have suggested that approximately 60,000 HIV-positive cases live in Iran. According to the previous hospital-based reports, respiratory failure and bloodstream infection are the main causes of ICU admission among HIV-infected individuals, respectively. However, bloodstream infection is responsible for 15–30% of all ICU admissions among HIV-infected patient, and the bloodstream infection rate among HIV-infected patient is more than 1,000 cases per 100,000 patients [1]. Despite the fact that the introduction of highly active antiretroviral therapy (HAART) promotes and improves the quality of life of HIV-infected patients, acquired immune deficiency syndrome (AIDS) as a serious threat to global public health often needs critical care support in ICU [5, 6]. Several risk factors contribute to the HIV-infected patients to be susceptible to bacterial infections, including deficiency in humoral and cell-mediated immunity, followed by low CD4+ lymphocyte count, phagocytic cell dysfunction, and skin and mucous membrane defects [7]. Therefore, HIV-infected patients may be predisposed to systemic bacterial infections such as bloodstream infection and more at risk of urinary tract infections (UTIs) [8-10]. However, as to the best of our knowledge, there are a few data on the prevalence, etiologic agents, and the antimicrobial susceptibility pattern of bloodstream and urinary tract infections among HIV- positive patients in this region. **Objectives:** The aim of this study was to determine the spectrum of bacterial etiology and antibacterial susceptibility pattern of bloodstream infection and UTIs in Iranian HIV-infected patients.

Materials and methods

This retrospective cross-sectional study was conducted on HIV/AIDS patients for a period of ten years from January 2005 to January 2015 at two major hospitals of Nemazee and Faghihi, affiliated to Shiraz University of Medical Sciences, southwestern Iran. During the study period, demographic and clinical information of HIV/AIDS patients suspected to bloodstream infection and UTIs were recorded based on the compatible clinical manifestations sought by the physicians. This study was approved by the Ethics Committee of Shiraz University of Medical Sciences and was in accordance with the declaration of Helsinki. However, the committee waived the informed consent, because only the medical records were used, and the details were also kept strictly confidential.

Specimens and bacterial identification:

Using sterile conditions, 2 - 5 mL venous blood samples were gained from HIV/AIDS patients by the attending nurses and injected in BACTEC™ blood culture bottles. All bottles were incubated at 37°C aerobically condition in the BACTEC™ system (Model: 9050 and 9120) (Becton Dickinson, NJ, USA) for seven consecutive days [11]. Standard bacteriological methods were used for the bacteria isolation and identification from subculture samples. Moreover, the midstream urine samples were collected in a clean container. Samples were cultured

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on blood agar or MacConkey agar (HiMedia, India) using a standard calibrated loop (0.01 mL), and the plates were incubated at 37°C for 24 hours. The grown bacteria were examined for colony morphology as well as Gram staining characteristics and were identified using standard microbiological methods.

Antimicrobial susceptibility testing: Antimicrobial susceptibility testing was performed for all bacterial isolates using disk diffusion method on Mueller-Hinton agar (Oxoid) according to the Clinical and Laboratory Standards Institute (CLSI) recommendations [12]. The selected antimicrobial disks (HiMedia, India) and the results interpretation for each pathogen were based on CLSI recommendations.

Statistical analysis: The analysis was performed using SPSS™ software, Version 21.0 (IBM Corp., USA). The results were presented as descriptive statistics in terms of relative frequency. Values were expressed as mean ± standard deviation (continuous variables) or the group percentage (categorical variables).

Findings

During a 10-year study period, out of 228 HIV-infected patients suspected to bloodstream infection and UTIs, 191 (83.8%) and 37 (16.2%) cases were male and female, respectively. Out of 228 collected samples, the number of culture-positive blood and urine specimens was 53 (n = 23.2%) and 22 (n=9.6%), respectively. Out of 53 culture-positive blood samples, the most frequent Gram-positive bacteria were *S. aureus* (N = 17, 32.1%) and *S. epidermidis* (N = 5, 9.4%), while the most frequent Gram-negative bacteria were *Pseudomonas* spp. (N = 5, 9.4%), *Salmonella non typhi* (N = 5, 9.4%), and *E. coli* (N = 4, 7.5%). Furthermore, among 22 culture-positive urine samples, the predominant Gram-positive bacterium was *Enterococci* spp. (N = 7, 31.8%), while *E. coli* (N = 5, 22.7%) was the most frequent Gram-negative bacterium. The detailed results of bacterial isolation from urine and blood cultures in HIV-infected patients are shown in Table 1.

Antibacterial susceptibility testing results indicated that among Gram-positive bacteria, *S. aureus* showed a high resistance against penicillin (100%) and tetracycline (76.5%), while the highest resistance of *Enterococci* was observed toward tetracycline (90%) and ampicillin (80%). In addition, the most effective antibiotic against *S. aureus* and *Enterococci* isolates was rifampin; meanwhile, among coagulase-negative *Staphylococci* (CoNS) isolates, chloramphenicol was the most effective antibiotic. *Enterobacteriaceae* and *Pseudomonas* spp. isolates showed a high level of resistance against tetracycline (88.2%) and aztreonam (72.7%), whereas the isolates were mostly susceptible to aztreonam (88.2%) and tobramycin (81.8%). The full results of antibiotic resistance patterns of Gram-positive and Gram-negative pathogens from blood and urine samples of HIV-positive patients are presented in Table 2.

According to the history of patients, 49 (21.5%) patients were co-infected by Hepatitis C virus, and 33 (14.5%) cases had a history of drug injection. Moreover, the mortality rate was 16.2%, and the remaining cases were discharged from hospitals.

Discussion

HIV causes AIDS and is a significant problem for global public health. AIDS as a disease has had economically a huge impact on communities and public health [13-14]. According to data reported by the WHO, the rate of AIDS epidemic in Iran is dramatically growing [15]; therefore, due to the high prevalence of opportunistic infections such as bloodstream infections (BSIs) and UTIs in these patients, the mortality rate has increased [2]. Therefore, routine surveillance

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Table 1) The detailed results of bacterial isolation among urine and blood cultures in HIV-infected patients

Isolate	HIV Positive		Total
	Urine	Blood	
Gram-positive	**10**	**30**	**40**
Staphylococcus aureus	-	17	17
Staphylococcus epidermidis	1	5	6
Enterococci	7	3	10
Pneumococci	-	2	2
Coagulase-negative staphylococci	1	1	2
Streptococci	1	-	1
Bacillus	0	2	2
Gram-negative	**12**	**23**	**35**
Escherichia coli	5	4	9
Pseudomonas spp.	2	5	7
Alcaligenes spp.	-	4	4
Salmonella non *typhi*	-	5	5
Enterobacter spp.	1	2	3
Klebsiella spp.	1	1	2
Citrobacter spp.	1	2	3
Acinetobacter spp.	2	-	2
Yeast	3	1	4
Candida non *albican*	5	-	5
Diphteroid	0	4	4

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Table 2) Antimicrobial susceptibility patterns of pathogens isolated from Blood and urine cultures

Bacteria	Antimicrobial Agent	Resistant No. (%)	Susceptible No. (%)
S. aureus (N = 17)	Penicillin	17 (100)	0
	Gentamicin	10 (58.8)	7 (41.2)
	Tetracycline	13 (76.5)	4 (23.5)
	Erythromycin	12 (70.5)	5 (29.5)
	Clindamycin	10 (58.8)	7 (41.2)
	Ciprofloxacin	7 (41.2)	10 (58.8)
	Rifampin	4 (23.5)	13 (76.5)
	Cefoxitin	7 (41.2)	10 (58.8)
	Co-trimoxazole	6 (35.2)	11 (64.8)
Streptococcus spp. (N = 3)	Erythromycin	2 (66.6)	1 (33.4)
	Ceftriaxone	1 (33.4)	2 (66.6)
	Clindamycin	2 (66.6)	1 (33.4)
	Chloramphenicol	0	3 (100)
	Penicillin	1 (33.4)	2 (66.6)
	Co-trimoxazole	1 (33.4)	2 (66.6)
	Vancomycin	0	3 (100)
Enterococci (N = 10)	Ampicillin	8 (80)	2 (20)
	Vancomycin	4 (40)	6 (60)
	Erythromycin	7 (70)	3 (30)
	Tetracycline	9 (90)	1 (10)
	Ciprofloxacin	5 (50)	5 (50)
	Rifampin	2 (20)	8 (80)
Coagulase negative *Staphylococci* (N = 8)	Ciprofloxacin	4 (50)	4 (50)
	Tetracycline	6 (75)	2 (25)
	Rifampin	3 (37.5)	5 (62.5)
	Erythromycin	5 (62.5)	3 (37.5)
	Chloramphenicol	0	8 (100)
	Gentamicin	3 (37.5)	5 (62.5)
	Penicillin	7 (87.5)	1 (12.5)
	Cefoxitin	5 (62.5)	3 (37.5)
	Co-trimoxazole	3 (37.5)	5 (62.5)

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Bacteria	Antimicrobial Agent	Resistant No. (%)	Susceptible No. (%)
Pseudomonas spp. (N =11)	Ciprofloxacin	4 (36.4)	7 (63.6)
	Amikacin	3 (27.3)	8 (72.7)
	Ceftazidime	4 (36.4)	7 (63.6)
	Aztreonam	8 (72.7)	3 (27.3)
	Imipenem	5 (45.4)	6 (54.6)
	Tobramycin	2 (18.2)	9 (81.8)
Salmonella non typhi (N =5)	Ciprofloxacin	0	5 (100)
	Ceftazidime	0	5 (100)
	Ampicillin	1 (20)	4 (80)
	Co-trimoxazole	0	5 (100)
	Chloramphenicol	0	5 (100)
Enterobacteriaceae (N =17)	Amoxicillin/clavulanat	5 (29.4)	12 (70.6)
	Aztreonam	2 (11.8)	15 (88.2)
	Cephalothin	12 (70.6)	5 (29.4)
	Cefoxitin	12 (70.6)	5 (29.4)
	Cefotaxime	13 (76.5)	4 (23.5)
	Ceftazidime	14 (82.3)	3 (17.7)
	Cefepime	12 (70.6)	5 (29.4)
	Tetracycline	15 (88.2)	2 (11.8)
	Gentamicin	12 (70.6)	5 (29.4)
	Ciprofloxacin	12 (70.6)	5 (29.4)
	Imipenem	13 (76.5)	4 (23.5)
	Co-trimoxazole	12 (70.6)	5 (29.4)
Acinetobacter spp. (N =2)	Imipenem	0	2 (100)
	Ciprofloxacin	0	2 (100)
	Ampicillin-sulbactam	1 (50)	1 (50)
	Ceftazidime	0	2 (100)
	Gentamicin	0	2 (100)
	Amikacin	1 (50)	1 (50)
	Tetracycline	0	2 (100)

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is necessary to determine the etiology of BSIs and UTIs in order to be able to choose appropriate therapy for the management of HIV-infected population.

In the present study, the rate of bacterial isolation from the examined blood samples was found to be 23.2%. This finding was relatively in accordance with the findings of other studies conducted in Malawi (23%), Cambodia (19%), and Tanzania (17%) [16-18]. However, the isolation rate in this study was higher than that reported by Mohammadnejad et al. (2010) (9.9 %) among HIV/AIDS hospitalized patient [19]. The present study results showed that the frequency of culture-positive urine samples was 15.7%. This finding was lower than those reported in Nigeria (40.4%) and USA (25%), but consistent with those reported in Iran (13.2%) and Ethiopia (14%) [20-22]. These variations in bacterial isolation rate suggest that some considerations such as differences in geographical distribution, diagnostic methods, infection control policies, and received clinical care or self-medication may have affected the obtained results.

In the present study, the most common bacterial agent of BSIs was *S. aureus,* followed by *Enterobacteriaceae*. Previously, several authors from the United States, Ethiopia, and Thailand reported that *S. aureus* was the main bacterial agent of bloodstream infection in HIV-infected patients, consistent with the present study results [23]. In addition, several studies reported that *Enterobacteriaceae*, particularly *E. coli* was the most prevalent Gram-negative pathogen in HIV/AIDS-infected patients [13, 24].

Based on the present study results, Gram-negative bacteria were found in 54.5% of patients with UTIs. Among these bacteria, *E. coli* was the most common species. Moreover, among Gram-positive pathogens, *Enterococci* strains were the most prevalent isolates. These findings were consistent with the findings of other studies showing *E. coli* and *Enterococci* as the most common uropathogenic bacteria [25].

In the present study, *S. aureus* isolates as the predominant agent of BSIs showed a high susceptibility toward rifampin and co-trimoxazole; 41.2% of which were MRSA, as well. In agreement with the present study findings, Ghassabi et al. (2017) showed that *S. aureus* isolates were completely susceptible to rifampin and co-trimoxazole, while they were resistant to penicillin G [26]. In addition, the antibiotic susceptibility pattern of other Gram-positive isolates such as *Enterococci* and CoNS revealed that most of the isolates were multidrug resistant (MDR), and only vancomycin and chloramphenicol were effective against them. Thus, these antibiotics could be considered as the drug of choice for empirical therapy of infections caused by these pathogens in this region.

Conclusion

In summary, this study results introduced *S. aureus* and *E. coli* as the most common causative agents of BSIs among HIV-infected patients in this region. Hopefully, some locally available antibiotics were effective against the majority of Gram-positive and Gram-negative bacteria isolated in this study. The present study findings highlighted the emergence and spread of opportunistic infections and high level of antibiotic resistance among HIV-infected patients; therefore, restricted infection control strategies must be pursued in these hospitals.

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