Urinary tract infection in Hemodialysis patients with renal failure

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Summary:

Background: Urinary tract infections (UTIs) are common in dialysis patients, are associated with increased rate of complications, and may be difficult to diagnose due to often subclinical presentation.

Objectives: To examine theprevalence of urinary tract infections in hemodialysis patients with renal failure, and to evaluate the diagnostic accuracy of pyuria as a screening test in hemodialysis patients.

Patients and Methods: A total of forty hemodialysis patients (27 males and 13 females) with renal failure were selected according to the study criteria. Clean-catch mid-stream urine specimens were obtained from study patients, their urinalysis and bacterial culture were performed according to standard techniques. Bacteriuria is defined as detection of $\geq 10^5$ cfu/ml of a single microorganismin culture of urine specimens.Pyuria is defined as the presence of ≥10 neutrophils per high power field of voided mid-stream urine.

Results: Urine from 25(62%) patients had no significant organism growth**,** whereasurine from 15(37%) patients grew $\geq 10^5$ cfu/ml; 6 patients had been infected with *E. coli*, 5 patients with Klebsiella spp., one patient with Acinetobacter, one patient with α-hemolytic Streptococci, one patient with coagulase negative Staphylococci, and one patient with Proteus spp.. Fourteenout of 40 (35%) patients had pyuria and only 9 (64%) out of 14 patients had a positive urine culture for infection. The sensitivity and specificity of pyuria screening for UTI was 60% and 80%, respectively. The positive and negative predictive values are 64% and 77%, respectively.

Conclusions: The result of this study demonstrates that pyuria was a good marker for significant bacteriuria in these patients. Cultural techniques are needed for susceptibility testing of bacterial isolates to guide antimicrobial therapy. The antimicrobial susceptibility tests in this study revealed that Amikacin, Gentamicin, Ceftazidime, Cefoxitin, and Imipenem act well on isolated bacteria.

Key Words: Hemodialysis, Urinary tract infection**,** Pyuria.

Introduction:

Dialysis is the process of removing waste products and excess fluids from the body. There are two types of dialysis: hemodialysis and peritoneal dialysis. In hemodialysis (HD), blood is removed from the body and pumped by a machine outside the body into a dialyzer (artificial kidney). Doctors decide to place a person on dialysis when the person's kidney failure is causing certain conditions such as uremic encephalopathy, pericarditis, acidosis, heart failure, pulmonary edema, and hyperkalemia [1]. For patients with end-stage renal disease (ESRD), renal replacement therapy is achieved by dialysis (hemodialysis or peritoneal dialysis) or kidney transplantation. Although true and complete replacement of renal function is not provided by dialysis, this modality removes metabolic wastes and excess body water, and replenishes body buffers in order to sustain life [2]. Urinary tract infections (UTIs) are common in dialysis patients, are Associates with increased rate of complications, and may be difficult to diagnose due to often subclinical presentation. Of special relevance is the limited diagnostic value of the presence of pyuria in the urinalysis, as pyuria is a common occurrence in dialysis patients (11-70%) and may be associated with the underlying etiology of the kidney disease rather than with the presence of infection [3]. In addition to infections associated with dialysis access devices, patients with end stage renal disease (ESRD) who require renal replacement therapy may be susceptible to non-access related infections. Diagnostic strategies for these infections are similar to those used for patients without renal failure. However, a higher index of suspicion and a lower threshold for the initiation of a search is appropriate, since patients with ESRD are frequently diabetic and/or immunosuppressed because of the retention of uremic toxins [4]. The clinical presentation of urinary tract infection in a dialysis patient with residual urine production is similar to that of an individual without renal failure. By comparison, anuric patients may present with only bladder discomfort and/or fever.The presence of pyuria, including white blood cell casts, without bacterial infection is common in dialysis patients. Some investigators have suggested that pyuria is a marker

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for urinary tract infection, even in asymptomatic dialysis-dependent patients. The literature is sparse and conflicting concerning this issue [5]. In spite of a large number of studies conducted for the investigation of UTIs in Iraq, little information regarding this issue in hemodialysis patients was provided. This study was planned to examine the prevalence of urinary tract infections in hemodialysis patients with renal failure, and to evaluate the diagnostic accuracy of pyuria as a screening test in hemodialysis patients.

Patients and Methods:

This cross-sectional study was conducted in the Center of Renal Diseases and Transplantation at Baghdad Medical City from the period of Nov. 2010 to Apr. 2011. A total of forty hemodialysis patients with renal failure were enrolled in this study. All patients were selected if they were on hemodialysis for more than one month and had a urinary output more than 30 ml between two dialysis sessions. Patients, who had an infectious disease, carcinoma, HIV, or were on medication inducing pyuria were excluded. All study patients were found under the following therapeutic schedule; Zylofen (1mg), One-alpha (1mg), Lasimex tablet, and Calcium tablet. Clean-catch midstream urine specimens were collected from study patients in a sterile container sent to the laboratory immediately. A typical medical urinalysis employing urine dip stick, microscopic examination and bacteriological culture were included according to standard methods.Bacteriuria is defined as detection of $\geq 10^5$ cfu/mlof a single microorganism in culture of urine specimens [6]. Pyuria is defined as the presence of ≥10 neutrophils per high power field of voided mid-stream urine as used by most studies that evaluated the diagnostic relevance of pyuria in dialysis patients [7].Bacterial culture growth was counted according to the number observed per plate, fewer than 10 colonies per plate represented $< 10^3$ cfu/ml, 10 to 100 colonies per plate represented 10^3 to 10^4cfu/ml, 100 to 1000 colonies per plate represented 10^4 to 10^5 cfu/ml, and > 1000 colonies per plate presented > 10^5 cfu/ml.Microorganisms isolated from all specimens were identified at species level according to standard microbiology methods, that's including: direct microscopic examination of gram stained preparations, biochemical profiling test, and antimicrobial susceptibility methods. The API 20 E system (bioMérieux Inc., France) represented a type of kit for rapid identification of bacterial isolates [6]. The antimicrobial susceptibility test was performed according to Kirby-Bauer (disk diffusion) technique using Muller-Hinton agar and different single antimicrobial discs supplied commercially. Results were read according to the National Committee for Clinical Laboratory Standards guidelines (NCCLS) [8]

Statistical analysis: Descriptive statistics were calculated for the cross-sectional population in this study. Accuracy parameters of pyuria that's including sensitivity, specificity, positive predictive value, and negative predictive value were calculated according to standard methods. All the statistical analysis was performed using SPSS computer program version 16 and Microsoft Excel application.

Results:

Demographic and clinical presentation of study patients are shown on table (1). The number of male patients was higher than that of females, 27 (67.5%) versus 13 (32.5%). The study revealed that 14 (35%) of patients were at the age rangeof 41-50 years. It was shown that 37 (92.5%) of the patients were with hypertension and 3 (7.5) with diabetes mellitus. Only 3 (7.5%) of study patients were detected with nephrotic syndrome, the remainder were with chronic renal failure 37 (92.5).

Table (1) Demographic and clinical presentation of study patients

Characteristics	(No.)	(%)
Male	27	67.5
Female	13	32.5
Age:		
• 10-20 years	6	15
• 21-30 Years	8	20
• 31-40 Years	7	17.5
• 41- 50 Years	14	35
• 51-60 Years	3	7.5
• > 60 Years	2	5
Current illness: Chronic renal failure	37	92.5
Nephrotic syndrome	3	7.5
Renal transplantation; HD* without transplantation	12	30
HD with successful transplantation	8	20
HD with rejected transplantation	8	20
HD with waiting transplantation	12	30
Underlying conditions: Diabetes Mellitus	3	7.5
Hypertension	37	92.5

* HD: Hemodialysis

Bacteriological examination revealed that urine from 25(62.5 %) patients had no significant organism growth**,** whereas 15(37.5 %) patients grew $\geq 10^5$ cfu/ml. Fourteen patients (35%) had pyuria and only nine (64%) of them had a positive urine culture for infection. Table (2) revealed thatthe isolation frequency of pathogenic bacteria was 15 (37.5%); 6(15%) patients had been infected with *E. coli*, 5(12.5%) patients with Klebsiella spp., and one (2.5%) with Acinetobacter, α-hemolytic Streptococci, coagulase negative Staphylococci, and Proteus spp.All *E. coli* and Klebsiella isolates were sensitive to Amikacin and resistant to Ampicillin (data not shown).

Table (2) Frequency of isolated bacteria from urine specimens of the study patients

Isolated bacteria	(No.)	(%)
Escherichia coli	6	15
Klebsiella spp.	5	12.5
Acinetobacter spp.	1	2.5
α- hemolytic Streptococci	1	2.5
Coagulase – ve Staphylococci	1	2.5
Proteus spp.	1	2.5
Total	**15**	**37.5**

The diagnostic accuracy of pyuriain the identification of a positive urine culture of ≥ 10^5 cfu/mlis shown in table (3).The sensitivity and specificity of pyuria screening for UTI was 60% and 80%, respectively. The positive and negative predictive values are 64% and 77%, respectively.

Table (3) Diagnostic accuracy of pyuria in the identification of a positive urine culture of ≥ 10^5 cfu/ml

Screening test	positive urine culture of ≥ 10^5 cfu/ml			
	Sensitivity	Specificity	Positive Predictive value	Negative Predictive value
Pyuria = ≥10 neutrophils per high power field	60 %	80 %	64 %	77 %

Discussion:

This study revealed that the number of male patients was higher than that of females, 27 (67.5%) versus 13 (32.5%). In addition, 14 (35%) of them were at the age rangeof 41-50 years. There is no supporting information dealing with the gender and age variation within this population in the literature. It was shown that 37 (92.5%) of the patients were with hypertension and only three (7.5%) were with diabetes mellitus. Other studies showed that the underlying disorder was diabetes mellitus in 50% and hypertension in 20% of patients on long term hemodialysis [9].

It was previously recorded that urinary tract infections (UTIs) are common in dialysis patients. The prevalence of UTIs in this study was 37.5% as indicated by positive urine culture of ≥ 10^5 cfu/ml. In addition, the prevalence of pyuria was 35% using the cutoff value of > 10 leukocytes per high-power field. These results are relatively similar to previous findings in the literature [3][10].Immune system disturbances and renal failure can predispose to common asymptomatic UTI in patients with dialysis [11]. This study was not planned to identify risk factors for developing a nosocomial infection among chronic hemodialysis patients. Instead, a cross-sectional study was conducted to estimate the old and new cases of asymptomatic UTI in hemodialysis patients, either nosocomially or community acquired in this population.

Patients with kidney failure are more prone to developing urinary tract infections for a number of reasons. First of all, the mere act of passing urine tends to flush out the urinary tract of infectious agents so they cannot gain a foothold and cause problems. Once the kidneys fail and the production of urine is decreased, this normal flushing action is gone. UTIs usually are caused by bacteria which normally inhabit the bowel and spread to the urinary tract by local extension. Patients with chronic kidney disease have abnormalities in their immune system which impair their ability to fight infection. Although the white blood cell count in the typical laboratory testing profile may be normal, the dialysis patient's white blood cells (which are the primary line of defense against infection) typically do not function normally [12].

The spread of infectious agents from the dialysis machine or procedure to the kidney patient is unusual in the setting of current infection control policies but does rarely occur. Even if the dialysate fluid is contaminated with an infectious agent, the dialyzer membrane material is an effective barrier to the spread of that agent from the machine to the patient's blood. Infections related to the dialysis treatment, although unusual, generally occur during the put-on or take-off process when infectious agents can be introduced into the patient's dialysis catheter or permanent vascular access because of improper sterile technique. Therefore, it is important for patients to become familiar with and insist that sterile technique be used during the beginning and ending of dialysis treatment. The antimicrobial susceptibility tests in this study revealed that Amikacin, Gentamicin, Ceftazidime, Cefoxitin, and Imipenem act well on isolated bacteria. Although Aminoglycosides are effective against many gram-negative bacteria, theymay be ototoxic and nephrotoxic, especially in patients with diminishedrenal function. Therefore, acute uncomplicated cystitis inwomen can be effectively and inexpensively treated, before the infectingorganism is known, with a three-day course of oral trimethoprim-sulfamethoxazole, fluoroquinolone. Otheralternatives include 5- to 7-day regimens of Nitrofurantoin, or a singledose of Fosfomycin. Acute uncomplicated pyelonephritis can often be managed with a 7-daycourse of an oral fluoroquinolone. Urinary tract infections that recur afteruse of antimicrobial agents or are acquired in hospitals or nursing homesare more likely to be due to antibiotic-resistant gram-negative bacilli, *S. aureus* or enterococci. A fluoroquinolone, oral Amoxicillin/Clavulanateor an oral third-generation cephalosporin such as Cefpodoxime, Cefdiniror Ceftibuten can be useful in treating such infections in outpatients. In hospitalized patients with urinary tract infections, treatment with a third generation cephalosporin, a fluoroquinolone, Ticarcillin/Clavulanate, Piperacillin/Tazobactam, Imipenem or Meropenem is recommended, sometimes together with an aminoglycoside such as Gentamicin, especiallyin patients with sepsis syndromes [13].

The diagnostic accuracy of pyuria in this population has been incompletely evaluated and is the object of this study. The sensitivity and specificity of pyuria screening for UTI in this study was 60% and 80%, respectively. The positive and negative predictive values are 64% and 77%, respectively. The link between pyuria and UTI has been previously evaluated and results have been controversial. Cabaluna and associates were the first group that studied the relationship between pyuria and UTI in patients on hemodialysis [14]. One study reported that pyuria was a good marker for detection of UTI; the authors showed that 70% of patients with a positive pyuria had a positive culture [10]. In contrast, one study reported that although a positive sample for pyuria had high sensitivity and negative predictive value, the low positive predictive value and specificity do not allow elimination ofthe need forurine culturing [9].

Conclusion:

The result of this study demonstrates that the urinary tract infection, even in asymptomatic patients, mayassociate with increased rate of complications. Pyuria was a good marker for significant bacteriuria in these patients. However, cultural techniques are needed for susceptibility testing of bacterial isolates to guide antimicrobial therapy. Nephrotoxic antibiotics should be weighed against their adverse effects in hemodialysis patients.

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