Zagazig University Medical Journal
www.zumj.journals.ekb.eg

https://doi.org/10.21608/zumj.2024.265983.3152 Volume 30, Issue 8.1, NOV. 2024, Supplement Issue

Manuscript ID: ZUMJ-2401-3148
DOI: 10.21608/ZUMJ.2024.266665.3148

ORIGINAL ARTICLE

Asymptomatic Urinary Tract Infections in Patients with End Stage Renal Disease on Regular Hemodialysis

Abdalla M. Nawara [1], Ahmed Abdulsaboor [2], Abdo El-Sayed Abd El-Rahem Ahmed [3], Heba Shafeak Abd El Khalik Hussein [1]

1 Internal Medicine Department, Faculty of Medicine, Zagazig University, Egypt
2 Clinical Pathology Department, Faculty of Medicine, Zagazig University, Egypt
3 M.B.B.C.H Faculty of Medicine, Zagazig University Egypt

Corresponding author:

Abdo El-Sayed Abd El-Rahem

Email:

eabdo9754@gmail.com.

Submit Date: 30-01-2024
Revise Date: 22-02-2024
Accept Date: 26-02-2024

ABSTRACT

Background: Isolation of a specific quantitative count of bacteria in an appropriately collected urine sample from a patient who does not exhibit any symptoms or signs indicative of an asymptomatic urinary infection. In this study, we aimed to estimate the correlation between the asymptomatic urinary tract infection and hemodialysis (HD)-dependent end-stage renal disease patients. **Methods:** Sixty patients with End Stage Renal Disease who were on long-term hemodialysis in this prospective cohort study were classified into 42 patients with positive pus in urine (70%) and 18 patients with non-pyuria (30%). Urina analysis, routine culture, and count of bacteria were assessed among other laboratory investigations in all patients. **Results:** Significant higher levels of erythrocyte sedimentation rate (ESR), C- reactive protein (CRP), and neutrophils levels among cases with pyuria versus cases with non-pyuria (p–value 0.032, 0.020, 0.046 respectively), the majority of culture and sensitivity are 11 patients (36.7%) for Levofloxacin followed by nine patients (30%) for Ciprofloxacin. Multivariate regression analysis revealed that the most significant predictors of pyuria were DM, SBP (mmHg), ESR (mm/hr), CRP (mg/L), Neutrophils and Decrease Hb (gm/dL) with [OR (C.I.95%), p-value] [[1.855 (0.505- 5.679), p= 0.024; 1.761 (0.244- 4.600), p= 0.029; 1.061 (0.969- 3.742), p= 0.036; 1.790 (0.457- 6.823), p= 0.022; 1.981 (0.895- 3.460), p= 0.040 and 1.730 (0.422- 5.384), p= 0.025], respectively. **Conclusion:** In asymptomatic urinary tract infection patients, pyuria was a good marker of significant bacteriuria. Asymptomatic bacteriuria was more prevalent in female patients, patients with elevated ESR, CRP, and neutrophils levels, high blood pressure, comorbidities and diabetes, and anemia.

Keywords: Asymptomatic Urinary Tract Infections, End Stage Renal Disease, Regular Hemodialysis.

INTRODUCTION

Dialysis is a method of filtering the blood and eliminating excess fluids and waste. Hemodialysis and peritoneal dialysis are the two main forms of this treatment. Hemodialysis, or HD, involves removing blood from the body and filtering it through a dialyzer using a machine that is located outside the body (artificial kidney) [1]. Dialysis is suggested by nephrologists when specific complications related to kidney failure occur, including pericarditis, uremic encephalopathy, heart failure, acidosis, hyperkalemia, and pulmonary edema [2]. Hospitalization due to infection ranks second in terms of death rate among hemodialysis patients. An immunocompromised state, resulting

from abnormalities in cellular immunity, neutrophil function, and the neutrophil response to infection, primarily increases the risk of infections, especially blood-borne pathogens, in these patients [3].

Asymptomatic bacteriuria, often known as an asymptomatic urinary infection, occurs when a specific quantitative count of bacteria is isolated from a urine sample taken from a healthy individual who does not exhibit any symptoms or signs that indicate a urinary infection. Pyuria is a sign of an inflammatory reaction in the urinary system, which is shown by an increase in the amount of polymorphonuclear leukocytes in the urine [4].

For a microbiologic diagnosis of asymptomatic bacteriuria, it is necessary to collect the urine specimen in a way that limits contamination and get it to the lab quickly enough to limit bacterial growth. The commonly accepted quantitative measurement is 105 colony-forming units per milliliter in two separate urine samples [5]. Antibiotic therapy is necessary for asymptomatic bacteriuria, which is a frequent complication among hemodialysis patients [6].These infections can be diagnosed using the same approaches as people who do not have renal failure. Due to the high prevalence of diabetes and immunosuppression in ESRD patients because of uremic toxin retention, it is reasonable to have a higher index of suspicion and a lower threshold for initiating a search [7]. In a patient with bacteriuria, whether it is symptomatic or asymptomatic, the diagnosis needs to be established by the presence of pyuria (≥10 leukocytes mm^{-3} of uncentrifuged urine) [8].

A common complication in hemodialysis patients is asymptomatic bacteriuria, which requires antibiotic treatment. For end-stage renal disease (ESRD) patients, the relevance of bacteriuria remains unknown. However, there is a lack of information on whether treating asymptomatic bacteriuria with HD reduces the incidence of UTIs in patients with end-stage renal disease.

Therefore, we did this work to estimate the incidence of asymptomatic urinary tract infection among hemodialysis-dependent end-stage renal disease patients, evaluate clinical picture changes in ESRD patients with asymptomatic UTI, and evaluate the relation between asymptomatic UTI and the number of HD sessions.

PATIENTS AND METHODS

Between December 2022 and December 2023, this prospective cohort study was carried out in the Internal Medicine Department, Faculty of Medicine, Zagazig University, nephrology unit, and Al-Ahrar Teaching Hospital nephrology unit on 60 patients who had End Stage Renal Disease and were long-term hemodialysis as part of this prospective cohort study.

Verbal and written informed consent were obtained from all participants after an explanation of the procedure and medical research. The research was conducted under the World Medical Association's Code of Ethics (Helsinki Declaration) for human research. This study was carried out after the approval of the Institutional Review Board (IRB) (#9501/22-6-2022).

Cases with the following criteria were included: age 18 or older who had End Stage Renal Disease on long-term regular hemodialysis (4 hours/day and three times a week) in the Dialysis Unit of the Internal Medicine Department at Zagazig University and Al-Ahrar Teaching Hospital, nephrology unit if they agreed to participate.

Cases with the following characteristics were excluded: cases who were younger than 18 years, Patients who received or have been receiving immuno- suppressive Therapy under any condition, e.g., history of transplantation or lupus erythematosus, patients who had a history of recent infection or antibiotics administration, patients whom it was difficult to obtain a urine sample from (as aneuric patient), and patients who had symptomatic UTI or Peritoneal dialysis.

All patients were subjected to Full history taking involving age, name, sex, history of medical diseases, duration of hemodialysis, and the cause of end-stage renal disease.

Complete clinical examination to exclude any hidden medical condition that may interfere with the results and diagnosis of hypertension was done based on when the systolic blood pressure (SBP) in the clinic was ≥140 mm Hg, and their diastolic blood pressure (DBP) is ≥90 mm Hg [9] or if the patient was known hypertensive and already under treatment. The patient's temperature was checked frequently for signs of infection or inflammation.

Laboratory investigations included Complete blood picture, Liver and kidney function tests, Complete Urine Analysis, Urine Culture and Antibiotic Sensitivity, serum uric acid and minerals (calcium and phosphorus), Random blood sugar (RBS), ESR, and CRP. Imaging studies included kidney ultrasonography. Follow-up was done for six months.

Patients were divided into two groups

Group I: Patients with pyuria (42 patients 70%), 30 patients with positive bacteriuria, and 12 patients with negative bacteriuria. Group II: Patients without pyuria (18 patients 30%).

Sample Collection

For blood tests, venous blood samples were collected by vein puncture under complete aseptic condition from every subject and then divided as follows:

For urine tests, all patients were instructed to collect midstream urine samples following the precautions required. Under aseptic conditions, a sterile, wide-mouth, screw-capped universal container was used to collect two consecutive samples of midstream urine: one after voided and one after clean-catch. The laboratory immediately sent the samples for microscopy, culture, and sensitivity testing.

STATISTICAL ANALYSIS

Using SPSS 24.0 for Windows, we gathered, tabulated, and statistically analyzed all the data (SPSS Inc., Chicago, IL, USA). The T-test or Mann-Whitney test was used to compare normally distributed continuous variables. Continuous Quantitative variables were expressed as the mean ± SD & median (range), and categorical qualitative variables were expressed as absolute frequencies (number) & relative frequencies (percentage). Data were checked for normality by using Shapiro Walk test. Using the chi-square test ($\chi 2$) and Fisher exact, the difference between the qualitative variables was estimated.

RESULTS

The patient's mean age was 59.73 ± 11.57 in the Pyuric group compared to 61 ± 11.58 in the Non-Pyuric group, with a p-value (p=0.665 NS). There was a higher frequency of DM as there were 24 patients (57.1%) in the Pyuric group compared to 3 patients (16.7%) in the non-group, with a p-value (p=0.004) (Table 1).

There was a statistically significant higher mean value of SBP as it was 152 ± 14.56 in the Pyuric group compared to 140.87 ± 10.11 for the non-Pyuric group, with a p-value (p=0.008). Also, the statistically significant lower mean value of DBP was 85.13 ± 11.7 in the Pyuric group compared to 91.93 ± 6.62 for the non-Pyuric group, with a p-value (p=0.035 S) (Table 2).

Table 3 showed that there was significantly higher ESR and CRP among cases in the **Pyuric group** versus cases in the Non-Pyuric group p–value 0.032 and 0.020, respectively, there was a highly statistically significantly higher value frequency of Pus cells (urinary WBCs/ HPF) in Pyuria group comparing to Non-Pyuria, with p-value (p<0.001) as well as a statistically significant higher mean value of Neutrophils which was 10.15 ± 4.98 in **Pyuric group** comparing to 7.47 ± 2.5 for Non-Pyuric group, with p-value (p=0.046 S). The recurrence was in 2 patients (2.8%) in the Pyuric group, while there was no recurrence in the non-Pyuric group. Still, there was an insignificant difference between groups, with a p-value (p=0.348).

Most of the culture sensitivity was 11 patients (36.7%) for Levofloxacin, followed by nine patients (30%) for Ciprofloxacin. The majority of bacteria detected in culture are:14 patients (46.7%) for E. coli, followed by six patients (20%) for Klebsiella SPP, then three patients for each of Proteus spp and Staphylococci, while there are 2 cases for each of Enterococcus SPP and streptococci. Most of the antibiotic resistance detected in culture was ampicillin for 11 patients (36.7%), followed by cefixime for nine patients (30%) and amoxicillin/clavulanic acid for nine patients (30%) (Table 4).

Most cases of positive bacteriuria, which were responding to treatment within seven days, were 14 cases (42%), and those responding to treatment within ten days were 8 cases (26.6%) while nonresponding to treatment were two cases (6.6%). The most sensitive antibiotics to E. coli were Levofloxacin, ciprofloxacin, and nitrofurantoin, while the most sensitive antibiotics to Klebsiella spp were gentamicin, ciprofloxacin, and nitrofurantoin. Also, the most sensitive antibiotics to Proteus spp were ceftriaxone and nitrofurantoin. At the same

time, the most sensitive antibiotic to Staphylococci was amikacin (Tables 5 and 6).

Multivariate regression analysis revealed that the most significant predictors of pyuria were DM, SBP (mmHg), ESR (mm/hr), CRP (mg/L), Neutrophils and Decrease Hb (gm/dL) with [OR (C.I.95%), p-value] [[1.855 (0.505- 5.679), p= 0.024; 1.761 (0.244- 4.600), p= 0.029; 1.061 (0.969- 3.742), p= 0.036; 1.790 (0.457- 6.823), p= 0.022; 1.981 (0.895- 3.460), p= 0.040 and 1.730 (0.422- 5.384), p= 0.025], respectively (Table 7).

Table 1: Comparison between the studied groups according to the demographic data, comorbidities, and anthropometric data

		Pyuria (N=42)	Non-Pyuria (N=18)	P. Value
Age (years)	**Mean±SD**	59.73 ± 11.57	61 ± 11.58	0.665
	Median (IQR)	61 (32-85)	61 (41-86)	
Sex				
Male		20 (47.6%)	12 (66.7%)	0.283
Female		22 (52.4%)	6 (33.3%)	
		Pyuria (N=42)	**Non-Pyuria (N=18)**	**P. Value**
DM		24 (57.1%)	3 (16.7%)	0.004*
HTN		19 (45.2%)	6 (33.3%)	0.396
Hepatic disease		2 (4.8%)	3 (16.7%)	0.130
Anthropometric measurements		**Pyuria (N=42)**	**Non-Pyuria (N=18)**	**P. Value**
Height (cm)	**Mean±SD**	165.82 ± 5.61	166.8 ± 5.78	0.598
	Median (IQR)	165 (155-180)	167 (160-175)	
Weight (kg)	**Mean±SD**	69.73 ± 9.22	70.6 ± 9.75	0.704
	Median (IQR)	70 (55-85)	70 (55-86)	
BMI [wt/(ht)^2]	**Mean±SD**	25.46 ± 3.06	25.29 ± 2.42	0.786
	Median (IQR)	25.7 (20.2-31.3)	25.1 (21.5-29.4)	
Obesity				
Normal weight		18 (42.9%)	7 (38.9%)	0.775
Overweight		19 (45.2%)	10 (55.6%)	0.464
Obese		5 (11.9%)	1 (5.6%)	0.460

DM: Diabetes mellitus, HTN: Hypertension, BMI: Body mass index . IQR: Interquartile range.

Using: t-Independent Sample t-test for Mean±SD.

x2: Chi-square test for Number (%) or Fisher's exact test, when appropriate

p-value >0.05 is insignificant; *p-value <0.05 is significant; **p-value <0.001 is highly significant

Table 2: Comparison between the studied groups according to vital signs

		Pyuria (N=42)	Non-Pyuria (N=18)	P. Value
Temperature(Co)	**Mean±SD**	37.01 ± 0.79	37.18 ± 0.9	0.447
	Median (IQR)	36.9 (35.7-38.6)	37.3 (35.7-38.6)	
SBP (mmHg)	**Mean±SD**	152 ± 14.56	140.87 ± 10.11	0.008*
	Median (IQR)	150 (128-175)	140 (127-160)	
DBP (mmHg)	**Mean±SD**	85.13 ± 11.7	91.93 ± 6.62	0.035*
	Median (IQR)	88 (60-105)	90 (82-104)	
MBP (mmHg)	**Mean±SD**	107.4 ± 10.58	105.53 ± 7.59	0.494
	Median (IQR)	108 (84-124)	103 (95-118)	

SBP: Systolic blood pressure, DBP: Diastolic blood pressure, MBP: Mean Blood Pressure

IQR: Interquartile range. Using: t-Independent Sample t-test for Mean±SD;

p-value >0.05 is insignificant; *p-value <0.05 is significant; **p-value <0.001 is highly significant

Table 3. Comparison between the studied groups according to kidney function test, ESR ,CRP Uric acid, and complications .

KFT		**Pyuria (N=42)**	**Non-Pyuria (N=18)**	**P. Value**
Creat (mg/dL)	**Mean±SD**	8.61 ± 1.25	8.73 ± 0.73	0.675
	Median (IQR)	8.62(2.3-11.17)	8.55(7.8-10.32)	
BUN	**Mean±SD**	88.18 ± 23.16	98.8 ± 19.47	0.108
	Median (IQR)	87 (48-150)	100 (66-130)	
Uric acid (mg/dL)	**Mean±SD**	8.95 ± 1.15	8.86 ± 0.78	0.691
	Median (IQR)	8.82 (6-12)	8.57(7.8-10.32)	
ESR (mm/hr)	**Mean±SD**	44.47 ± 19.5	30.2 ± 29.35	0.032*
	Median (IQR)	40 (18-95)	17 (4-85)	
CRP (mg/L)	**Mean±SD**	73.88 ± 89.03	19.22 ± 12.78	0.020*
	Median (IQR)	43.05(14.2-556.31)	21.3 (2.7-41.55)	
Urine analysis		**Pyuria (N=42)**	**Non-Pyuria (N=18)**	**P. Value**
PTN				
Nil		30 (71.4%)	9 (50.0%)	0.114
Positive +		9 (21.4%)	7 (38.9%)	0.164
Positive ++		3 (7.1%)	2 (11.1%)	0.609
RBCs		**16 (38.1%)**	**7 (38.9%)**	**0.954**
PUS (urinary WBCs/ HPF)				
0-2		0 (0.0%)	10 (55.6%)	<0.001**
3-4		0 (0.0%)	8 (44.4%)	
5-10		2 (4.8%)	0 (0.0%)	
10-20		5 (11.9%)	0 (0.0%)	
20-30		2 (4.8%)	0 (0.0%)	
30-40		3 (7.1%)	0 (0.0%)	
40-50		5 (11.9%)	0 (0.0%)	
50-60		7 (16.7%)	0 (0.0%)	
60-70		7 (16.7%)	0 (0.0%)	
70-90		3 (7.1%)	0 (0.0%)	

>100		8 (19.0%)	0 (0.0%)	
Nitrite		**3 (7.1%)**	**0 (0%)**	**0.215**
CBC		**Pyuria (N=42)**	**Non-Pyuria (N=18)**	**P. Value**
WBCs	**Mean±SD**	13.42 ± 6.09	10.62 ± 4.27	0.097
	Median (IQR)	14.3 (4.3-24.7)	9 (6.2-20)	
Neutrophils	**Mean±SD**	10.15 ± 4.98	7.47 ± 2.5	0.046*
	Median (IQR)	10.1 (3.1-21)	7 (2.3-11.7)	
Monocytes	**Mean±SD**	0.26 ± 0.3	0.19 ± 0.21	0.374
	Median (IQR)	0.2 (0-1.1)	0.1 (0-0.7)	
Eosinophils	**Mean±SD**	0.04 ± 0.07	0.03 ± 0.06	0.536
	Median (IQR)	0 (0-0.3)	0 (0-0.2)	
Basophils	**Mean±SD**	1.04 ± 1.94	1.24 ± 3.09	0.713
	Median (IQR)	0.6 (0-12.2)	0.3 (0-12.2)	
Lymphocytes	**Mean±SD**	1.57 ± 2.41	0.85 ± 0.53	0.233
	Median (IQR)	1 (0.2-12.2)	0.6 (0.2-2.3)	
RBCS	**Mean±SD**	4.37 ± 0.65	4.55 ± 0.81	0.345
	Median (IQR)	4.3 (2.8-6.4)	4.7 (2.7-5.9)	
Hematocrit	**Mean±SD**	33.21 ± 6.1	34.71 ± 4.46	0.396
	Median (IQR)	33.8 (24-46.7)	34 (25.4-41.4)	
Hb (gm/dL)	**Mean±SD**	11.46 ± 1.56	12.43 ± 1.68	0.043*
	Median (IQR)	11.9 (8.4-14.9)	12.5 (8.4-14.9)	
MCV	**Mean±SD**	80.7 ± 6.43	78.87 ± 6.48	0.310
	Median (IQR)	81 (72-96.8)	75 (72.6-96.8)	
MCH	**Mean±SD**	26.63 ± 2.21	26.23 ± 2.57	0.520
	Median (IQR)	25.3 (23.5-31.8)	25 (23.5-31.8)	
MCHC	**Mean±SD**	32.35 ± 1.54	32.56 ± 1.6	0.674
	Median (IQR)	32 (29-35.4)	32.8 (30-35.2)	
Platelets	**Mean±SD**	249.24 ± 112.15	208.07 ± 95.77	0.193
	Median (IQR)	230 (55-591)	200 (26-395)	
Complications	**Pyuria (N=42)**	**Non-Pyuria (N=18)**		**P. Value**
Recurrence	2 (4.8%)	0 (0.0%)		0.348

KFT: Kidney function tests, BUN: Blood urea nitrogen, Create: Creatinine, ESR: Erythrocyte sedimentation rate, CRP: C reactive protein, PTN: Protein, RBCS: Red blood cells, Pus: Pus Cells in Urine, CBC: Complete blood count, HB: Hemoglobin, MCV: Mean corpuscular volume, MCH: Mean corpuscular hemoglobin, MCHC: Mean corpuscular hemoglobin concentration

IQR: Interquartile range

Using: t-Independent Sample t-test for Mean±SD;

x2: Chi-square test for Number (%) or Fisher's exact test, when appropriate

p-value >0.05 is insignificant; *p-value <0.05 is significant; **p-value <0.001 is highly significant

Table 4: Microbiological evaluations in Pyuria group.

	Pyuria and positive culture (N = 30)	
	No.	**%**
Isolated Colony Sensitive to		
Levofloxacin	11	36.7%
Ciprofloxacin	9	30.0%
Nitrofurantoin	7	23.3%
Gentamicin	7	23.3%

	Pyuria and positive culture (N = 30)	
	No.	No.
Ceftriaxone	7	23.3%
Amikacin	5	16.7%
Trimthoprim/ Sulfamethoxazole (Co-timoxazole)	5	16.7%
Meropenem	4	13.3%
Imipenem	4	13.3%
Amoxacillin/ claviulinic acid	2	6.7%
Linazolid	2	6.7%
Cefuroxime	1	3.3%
Clindamycin	1	3.3%
Vancomycin	1	3.3%
Cefotaxime	1	3.3%
Isolated micro-organism		
E. coli	14	46.7%
Klebsialla spp	6	20.0%
Proteus spp	3	10.0%
Staphyloccocci	3	10.0%
Enterococcus spp	2	6.7%
Streptococci	2	6.7%
Isolated Colony Resistent to		
Ampicillin	11	36.7%
Cefixime	9	30.0%
Amoxacillin/ Claviulinic acid	9	30.0%
Nitrofurantoin	5	16.7%
Ampicillin/ sulbactam	6	20.0%
Ceftriaxone	5	16.7%
Co-trimoxazole	5	16.7%
Tobramycin	3	10.0%
Levofloxacin	3	10.0%
Gantamicin	2	6.7%
Cefoperazone/Sulbactam	2	6.7%
Ciprofloxacin	2	6.7%
Cefotaxime	1	3.3%
Cefopera Zone	1	3.3%
Ofloxacin	1	3.3%
Cefoclor	1	3.3%
Amikacin	2	6.7%
Cloxacillin	1	3.3%
Vancomycin	1	3.3%
Cefebime	1	3.3%

Table5: Duration of treatment and response to antibiotic therapy for positive bacteriuria.

Duration of antibiotic therapy	Number of patients of positive bacteriuria (n= 30)	Responding to treatment and resistance or recurrence	x2
3—5 days	6 (20.0%)	Responding	11.000
7days	14 (42%)	Responding	27.000
10 days	8 (26.6%)	Responding	15.000
Two weeks	2(6.6%)	Not responding	0.0000

Table 6: Antibiotic Sensitivity pattern of gram positive and gram-negative isolation

Antibiotic		E.coli n= 14	Klebsiella spp n=6	Proteus spp n=3	Staphylococci n=3	Enterococcus spp n=2	Streptococci n=2
Levofloxacin	**R** **S**	2(14.2%) 6(42.8%)	1(16.7%) 1(16.7%)	0 (0%) 1(33.3%)		0 (0%) 1(50.0%)	0 (0%) 2 (100%)
Ciprofloxacin	**R** **S**	0(0%) 5(35.7%)	2(33.3%) 2(33.3%)	0 (0%) 2(66.6%)			
Nitrofurantoin	**R** **S**	3(21.4%) 5(35.7%)	1(16.7%) 2(16.7%)				1(50.0%) 0 (0%)
Gantamicin	**R** **S**	1(7.1%) 3(21.4%)	0(0%) 3(50%)	1(33.3%) 0(0%)	0 (0%) 1(33.3%)		
Ceftriaxone	**R** **S**	3(21.4%) 0(0%)	0(0%) 2(33.3%)	0 (0%) 3(100%)		2(50.0%) 0 (0%)	0 (0%) 2 (100%)
Amikacin.	**R** **S**	1(7.1%) 2(14.2%)	1(16.7%) 1(16.7%)		0 (0%) 2(66.6%)		
Co– trimoxazole	**R** **S**	1(7.1%) 5(35.7%)	1(16.7%) 0(0%)		3 (100%) 0 (0%)		
Meropenem	**R** **S**	0(0%) 2(14.2%)	0(0%) 2(33.3%)				
Imipenem	**R** **S**	0(0%) 3(21.4%)		0(0%) 1(33.3%)			
Amoxacillin /claviulinic acid	**R** **S**	5(35.7%) 0(0%)	3(50.0%) 0(0%)	0(0%) 1(33.3%)		0 (0%) 1(50.0%)	1(50.0%) 0 (0%)
Linazolid	**R** **S**					0 (0%) 2 (100%)	
Cefuroxime	**R** **S**	0(0%) 1(7.1%)					
Clindamycin	**R** **S**	0(0%) 1(7.1%)					
Vancomycin	**R** **S**				0(0%) 1(33.3%)	1(50.0%) 0 (0%)	
Ampicillin	**R** **S**	9(64.3%) 0(0%)				2 (100%) 0 (0%)	
Tobramycin	**R** **S**	3(21.4%) 0(0%)					
Cefoperazone/sulbactam	**R** **S**	2(14.2%) 0 (0%)					
Cefotaxime	**R** **S**	1 (7.1%) 1 (7.1%)					
Cefoperazone	**R** **S**	1 (7.1%) 0(0%)					

Antibiotic		E.coli n= 14	Klebsiella spp n=6	Proteus spp n=3	Staphylococci n=3	Enterococcus spp n=2	Streptococci n=2
Ofloxacin	**R**				1(33.3%)		
	S				0 (0%)		
Cefaclor	**R**				(33.3%)		
	S				0 (0%)		
Cloxacillin	**R**						1(50.0%)
	S						0 (0%)
Cefebime	**R**				1(33.3%)		
	S				0 (0%)		
Ampicillin/ sulbactam	**R**	1 (7.1%)	2(33.3%)	3 (100%)			
	S	0(0%)	0(0%)	0(0%)			
Cefixime	**R**	6(42.3%)	2 (33.3%)		1(33.3%)		
	S	0 (0%)	0 (0%)		0 (0%)		

Table (7): Multivariate logistic regression model of independent predictors for Pyuria.

Items	β	Wald	Sig.	OR	95% C.I.	
					Lower	Upper
Age (years)	0.257	1.416	0.152	1.749	1.149	2.858
Sex	0.236	1.410	0.236	1.637	1.078	2.572
Obesity	0.570	0.739	0.636	0.452	0.133	1.123
DM	1.611	7.647	0.016*	1.855	0.505	5.679
HTN	1.639	0.874	0.519	0.676	0.203	1.541
Hepatic disease	0.184	0.950	0.352	1.416	1.011	2.233
Temperature (C°)	0.962	0.836	0.540	0.569	0.154	1.310
SBP (mmHg)	0.716	4.230	0.025*	1.761	0.244	4.600
DBP (mmHg)	0.377	0.707	0.725	0.424	0.112	1.051
MBP (mmHg)	0.267	1.473	0.143	1.819	1.195	2.972
ALT (IU/dL)	0.246	1.467	0.222	1.702	1.122	2.675
AST (IU/dL)	0.593	0.769	0.598	0.470	0.138	1.168
Albumin (gm/dL)	1.705	0.909	0.488	0.703	0.211	1.603
Fasting BG (mg/dL)	0.191	0.988	0.330	1.473	1.051	2.322
Creat (mg/dL)	1.000	0.870	0.507	0.592	0.160	1.362
BUN	0.925	0.804	0.574	0.547	0.148	1.259
Uric acid (mg/dL)	0.363	0.680	0.772	0.408	0.108	1.011
ESR (mm/hr)	0.412	3.865	0.029*	1.061	0.969	3.742
CRP (mg/L)	1.431	6.567	0.022*	1.790	0.457	6.823
Duration on hemodialysis (years)	0.393	0.736	0.682	0.441	0.117	1.093
Average of dialysis hours/week	0.278	1.532	0.135	1.892	1.243	3.091
Urine output (mL/24h)	0.255	1.525	0.208	1.771	1.166	2.782
Pus in urine	0.616	3.108	0.036*	3.489	1.144	5.215
Protein	1.773	0.945	0.458	0.731	0.219	1.667
Pus cells	0.199	1.027	0.311	1.532	1.093	2.415
WBCs	1.040	0.904	0.477	0.615	0.166	1.417
Neutrophils	0.381	2.649	0.040*	1.981	0.895	3.460
Monocytes	0.408	0.765	0.641	0.459	0.122	1.137
Eosinophils	0.289	1.593	0.126	1.968	1.293	3.215
Basophils	0.266	1.586	0.196	1.841	1.213	2.893
Lymphocytes	0.641	0.832	0.529	0.509	0.150	1.263

Items	β	Wald	Sig.	OR	95% C.I.	
					Lower	Upper
RBCS	1.844	0.983	0.431	0.760	0.228	1.734
Hematocrit	0.292	1.609	0.142	1.987	1.305	3.246
Decrease Hb (gm/dL)	1.323	5.072	0.024*	1.730	0.422	5.384
MCH	1.862	0.992	0.481	0.768	0.230	1.750
MCHC	0.209	1.078	0.327	1.609	1.148	2.536
Platelets	1.092	0.949	0.501	0.646	0.174	1.488

DM: Diabetes mellitus, HTN: Hypertension, BMI: Body mass index, SBP: Systolic blood pressure, DBP: Diastolic blood pressure, MBP: Mean Blood Pressure, KFT: Kidney function tests, BUN: Blood urea nitrogen, Create: Creatinine, ESR: Erythrocyte sedimentation rate, CRP: C reactive protein, PTN: Protein, RBCS: Red blood cells, Pus: Pus Cells in Urine, CBC: Complete blood count, HB: Hemoglobin, MCV: Mean corpuscular volume, MCH: Mean corpuscular hemoglobin, MCHC: Mean corpuscular hemoglobin concentration

β: Regression coefficient, SE: Standard error, CI: Confidence interval

DISCUSSION

When it comes to bacteria, the most frequent infection in humans is a urinary tract infection. It may or may not cause any noticeable symptoms at all. From minor irritative voiding symptoms to more severe complications, including bacteremia, sepsis, and even death, there is a vast range of morbidity associated with symptomatic infection. Asymptomatic urinary tract infection is characterized by the presence of bacteria in urine at quantitative counts indicative of infection, without localized genitourinary symptoms or any systemic symptoms that can be linked to the infection [10]. The utilization of pyuria as a marker of UTI in hemodialysis-dependent patients is controversial. The value of pyuria in immunosuppressed hemodialysis patients is unclear Almaiman L et al. [11]

This study aimed to reduce the complications of asymptomatic urinary tract infection in patients with end-stage renal disease on regular hemodialysis. The objectives of this study were to estimate the incidence of asymptomatic urinary tract infection among patients who had hemodialysis-dependent end-stage renal disease and to evaluate clinical picture changes in ESRD patients with asymptomatic UTI.

The participants in this study were 60 adults with a history of end-stage renal disease who were receiving long-term hemodialysis treatments at the dialysis unit of the internal medicine department at Zagazig University and the nephrology unit at Al-Ahrar Teaching Hospital. Out of the total number of patients, 42 had pyuria (about 70%) and were without pyuria (30 percent). In the present study, we found

that the incidence of pyuria in asymptomatic hemodialysis dialysis patients represented (70%), and non-pyuria (30%).

These findings were approximately in agreement with Orlowska et al. [12], who revealed that pyuria was present in 67% of asymptomatic hemodialysis patients with positive urine cultures. Also, the results of the present study agreed with Nicolle LE et al. [13], who reported that pyuria was present among 28% to 72% of dialysis patients.

This contrasted with Saber et al. [14], who found that the prevalence of pyuria was recorded as 38% and 0% in the ESRD patients' group and controls, respectively. This agrees with Eisinger et al. [15], who stated that hemodialysis patients have compromised immunity and are at high risk of UTI**.** Orlowska et al. [12] have also reported that Patients on continuous ambulatory peritoneal dialysis may be at increased risk for urinary tract infections (UTIs) due to renal failure and immune system disturbances. Another study by Yamashita et al. [16] revealed that of the 150 urine samples taken from CRF patients, 39 (or 26 percent) tested positive for culture, while 111 (or 74% of the total) tested negative.

In the current study, we found that there were insignificant differences between cases with positive pus and negative pus on urine regarding demographic data, with p-value (p>0.05); the mean age was 59.7 years in positive pus vs. 61 years in negative pus group, while male /female was 47.6%\52.4% in positive pus group vs. 66.7%/33.3% respectively. The Mean BMI was 25.4 vs 25.2, respectively, in two groups. As regards our study, obese patients represented (11.9%) of the Pyuric group and (5.6%) of non Pyuric group.

According to Yamashita K.et al. [16], the percentage of female patients with normosthenuria was 34.8%, while the rate of female patients with UTI was 61.5%. These results agreed with those findings. Patients with UTIs were more likely to be female than those with normosthenuria, according to the statistical analysis. The female anatomy may contribute to the higher incidence of UTIs in female patients [17].

On the other hand, Richa et al. [18] found that Patients between the ages of 61 and 70 had the highest frequency of culture-positive results. Out of 150 samples, 39 tested positive, with men making up 76.9% (30/39) and females 23.1% (9/39). The age group of 61–70 years old had the highest rate of cultural positivity among the female population, at 33.3%. There may be a higher number of male patients with chronic renal failure included in the study, which could explain why there was no statistically significant association.

Kwon et al. [19] revealed that the prevalence of ASP increases as the stage of chronic kidney disease advances. It was 51.4% (36.1% in men and 67.6% in women) in the 70 HD patients and 24.1% (14.0% in men and 41.2% in women) in the 228 non-dialysis CKD patients. In addition to Almaiman et al. [11] results showed that In comparison to the 164 CKD patients who did not have pyuria, 21.8% of them did, with a considerably higher proportion of females (68.9% vs. 28.6%) and a smaller percentage of men (31.1 percent vs. 71.4 percent). Patients with pyuric CKD had similar mean ages to those without pyuria. In contrast, 36.6% of patients with pyuria had stage 4 chronic kidney disease (CKD), while only 11.9% of individuals without pyuria had this stage of the disease (p = 0.002). Having pyuria in CKD patients may be a diagnostic indicator of advanced CKD, according to this study.

Patients with chronic kidney disease may experience polyuria due to inflammation of the renal parenchyma. Factors such as age, gender, diabetes, low albumin levels, and urinary tract infections (UTIs) can make this inflammation worse [20]. Comorbidities, which include diabetes, urinary tract blockage, and advanced age, all enhance the likelihood of UTIs; thus, the presence of UTIs in certain CKD patients may be a harmful consequence of these conditions [21]. The reduction of cellular and humoral immunity that occurs in CKD makes it a potential risk factor for UTI.[22].

In the current study, we found that as regards comorbidities, diabetes was found to be higher among cases with pyuria than non-pyuria, 57.1% vs 16.7%, respectively, with a p-value of 0.004. Our results were in concordance with the study of Kwon et al. [18] as they revealed that the pyuric group had higher rates of co-morbid diabetes (64.8 percent vs. 48.3 percent, P=0.011), higher levels of high sensitivity C-reactive protein (CRP), lower levels of hemoglobin and albumin (Alb), and more hematuria and proteinuria than the non-pyuric group.

In the present study, there was a significantly higher ESR (44.4vs 30.2), CRP (73.8 vs. 19.2), and neutrophils level (10.5 vs. 7.4) among cases with pyuria versus cases with non-pyuria p – value 0.032,0.020,0.046 respectively. As regards complete blood count, there was a significantly lower Hb level (11.4 vs 12.4) among cases with pyuria versus cases with non-pyuria, with a p-value of 0.043.

As regards our study, we found that the presence of urinary nitrites was (7.1%) in the public group and (0%) in the non-price group with p–a value (p >0.05). The pyuric and non-pyuric groups were not different in terms of median age. Essential factors for UTIs in the univariate analysis included sex, CKD classification, urine WBC count and distribution, and urinary nitrite presence. The presence of urine nitrites, proportion of neutrophils, and degree of pyuria were still independently related to more

significant risks of UTI in multivariate analysis [19].

Also, Almaiman L et al. [11] revealed that the prevalence of proteinuria, also known as albuminuria, was considerably greater in pyuric CKD patients compared to non-pyuric CKD patients (p = 0.001). A higher percentage of patients in the pyuric group compared to the non-pyuric group have late-stage chronic kidney disease (CKD), which is correlated with elevated blood urea (p = 0.006) and creatinine (p = 0.001) levels, as well as the prevalence of proteinuria (64%).

The present study showed that there was a highly statistically significantly higher value frequency of Pus cells (urinary WBCs/ HPF) in the Pyuria group compared to Non-Pyuria, with a p-value (p<0.001). This was in line with what Almaiman et al. [11] study found, as there was a statistically significant difference between the proportion of patients with pyuria and those without (67.7 percent vs. 2.4 percent; p = 0.002).

Our findings corroborated those of Ozdem et al. [23], who found a substantially greater prevalence of ASP in diabetic patients—both male and female—compared to the non-diabetic population (12.2 percent vs. 3.4 percent) and (21.4 percent vs. 8.7 percent), respectively.

In the present study, we found that there was a statistically significant higher frequency of recurrence of asymptomatic UTI in the Pyuric group compared with non Pyuric group (2.8% vs. 0%), respectively, with a p-value (p=0.348). These findings agreed with Taweel et al. [24], who revealed that Eleven patients, or 16.2%, experienced bacteriuria again within six months after the initial episode. Recurrence of bacteriuria was 25% in females and 0% in males, according to independent analysis (P = 0.006). There was no correlation between bacteriuria recurrence and age, race, ethnicity, kidney disease type, pyuria presence, symptoms, Charlson index, colony count, or polymicrobial bacteriuria. The rate of bacteriuria recurrence was not significantly different between individuals who were given antibiotics and those who were not (13.6 percent vs. 20.8 percent, P = 0.5). Results for both symptomatic and asymptomatic patients were comparable when analyzed as subgroups.

In the current study, we found that most of the culture #sensitivity is 11 patients (36.7%) for Levofloxacin, followed by nine patients (30%) for Ciprofloxacin. Most bacteria detected in culture are14 patients (46.7%) for E. coli, followed by six patients (20%) for Klebsiella SPP, then three patients for each of Proteus spp and Staphylococci, while there are 2 cases for each of Enterococcus SPP and streptococci. Most of the antibiotic resistance detected in culture is ampicillin for 11 patients (36.7%), followed by cefixime for nine patients (30%) and amoxicillin/clavulanic acid for nine patients (30%).

Similarly, El Nekidy et al. [25] found that **t**he causative organisms of UTI, most of the microorganisms found in the urine cultures were Escherichia coli (35%), Klebsiella spp. (14.3%), and Enterococci spp. (14.3%). Furthermore, among the organisms, 23 (41.1 percent) were Enterobacterales that produced extended-spectrum beta-lactamase. At diagnosis, 40 additional individuals (or 71.4% of the total) had more than 100,000 colonies. Drugs used to treat UTIs, how often to take them, and what dosages are recommended. Fifteen cases (26.8% of the total) used ertapenem 500 mg IV daily, whereas eight cases (14.3%) used ciprofloxacin 400/500 mg IV or oral daily.

Also**,** Saber et al. [14] found that E. coli was the most common bacterial strain found in infected dialysis patients (31.5%). Klebsiella spp. (Oxytocea and Pneumoniae), Proteus mirabilis, Mecithillin-resistant Staphylococcus aureus (MRSA), Staphylococcus aureus, and Enterococcus gallinarum were also detected in infected patients' urine (21%, 16%, 10.5%, and 10.5%, 10.5% respectively). Another study by Almaiman et al. [10] revealed that We found 2 cases of UTI among our 164 patients with pyuric CKD, accounting for 13.4% of the total. Ten out of twenty-two (45.5 percent) UTI patients had Escherichia coli as their causal agent. There have been reports of various additional bacteria that might cause UTIs.

Limitations

The current study was done in one center on a relatively small sample size, so additional research is required, including longer follow-up

and multicenter practice. To better understand our findings and to find factors that contribute to the worsening of renal illness, more randomized controlled trials with more extensive samples and more extended follow-up periods are required. To determine whether ACE/ARB with aldosterone antagonists can alleviate the renal disease load in this high-risk group of patients, more research is needed.

Author contribution: All authors contributed to the study. AM was responsible for selecting the subject, AAS was accountable for laboratory revisions and analysis, AEA was responsible for data collection, statistical analysis, and initial writing, and HSA was responsible for collecting the data of the studied cases and all shared for the formulation of the study design, editing, revision, and preparation of the final manuscript.

CONCLUSION

Asymptomatic bacteriuria was more prevalent in female patients, patients with elevated ESR, CRP, and neutrophils levels, high blood pressure, comorbidities and diabetes, and anemia.

It is possible that sterile pyuria in chronic kidney disease (CKD) patients can be predicted by analyzing the quantity and distribution of white blood cells (WBCs) in the urine. Antimicrobial susceptibility testing of bacterial isolates, however, requires culture procedures. In hemodialysis patients, the risks and benefits of nephrotoxic antibiotics should be considered.

CONFLICTS OFINEREST

No potential conflict of interest was reported by the authors.

REFRENCES

1. Norden CW, Kass EH. Bacteriuria of pregnancy--a critical appraisal. Annu Rev Med. 1968;19:431-70.
2. Müller V, Becker G, Delfs M, Albrecht KH, Philipp T, Heemann U. Do urinary tract infections trigger chronic kidney transplant rejection in man?. *J Urol*. 1998;159(6):1826-9.
3. Karkar A, Bouhaha BM, Dammang ML. Infection control in hemodialysis units: a quick access to essential elements. *Saudi J Kidney Dis Transpl*. 2014;25(3):496-519.
4. Cortes-Penfield NW, Trautner BW, Jump RLP. Urinary Tract Infection and Asymptomatic Bacteriuria in Older Adults. *Infect Dis Clin North Am*. 2017;31(4):673-88.
5. Nicolle LE, Bradley S, Colgan R, Rice JC, Schaeffer A, Hooton TM;et al. Infectious Diseases Society of America guidelines for the diagnosis and treatment of asymptomatic bacteriuria in adults [published correction appears in Clin Infect Dis. 2005 May 15;40(10):1556]. *Clin Infect Dis*. 2005;40(5):643-54.
6. Müller V, Becker G, Delfs M, Albrecht KH, Philipp T, Heemann U. Do urinary tract infections trigger chronic kidney transplant rejection in man?. *J Urol*. 1998;159(6):1826-9.
7. Levey AS, de Jong PE, Coresh J, El Nahas M, Astor BC, Matsushita K,et al. The definition, classification, and prognosis of chronic kidney disease: a KDIGO Controversies Conference report [published correction appears in Kidney Int. 2011 Nov;80(9):1000] [published correction appears in Kidney Int. 2011 1;80(9):1000]. *Kidney Int*. 2011;80(1):17-28.
8. Hooton TM, Scholes D, Stapleton AE, Roberts PL, Winter C, Gupta K,et al. A prospective study of asymptomatic bacteriuria in sexually active young women. *N Engl J Med*. 2000;343(14):992-7.
9. Schmidt BM, Durao S, Toews I, Bavuma CM, Hohlfeld A, Nury E, et al. Screening strategies for hypertension. *Cochrane Database Syst Rev*. 2020;5(5):CD013212.
10. Kamei J, Yamamoto S. Complicated urinary tract infections with diabetes mellitus. *J Infect Chemother*. 2021;27(8):1131-6.
11. Almaiman L, Allemailem KS, El-Kady AM, Alrasheed M, Almatroudi A, Alekezem FS, et al. Prevalence and Significance of Pyuria in Chronic Kidney Disease Patients in Saudi Arabia. *J Pers Med*. 2021;11(9):831.
12. Orlowska A, Majdan M and Koziol-Montewka M . Asymptomatic bacteriuria in patients on continuous ambulatory peritoneal dialysis. Ann Univ Mariae Curie Sklodowska.2002;; 57: 285-9
13. Nicolle LE. Asymptomatic bacteriuria: when to screen and when to treat. *Infect Dis Clin North Am*. 2003;17(2):367-94.
14. Saber M, Aboul Fadl LA, Helmi H, El Dobaa E, Waked E, El Shamaa A, et al. EJMM- [The]. 2009; 18 (3): 29-36.
15. Eisinger RP, Asghar F, Kolasa C, Weinstein MP. Does pyuria indicate infection in

asymptomatic dialysis patients?. *Clin Nephrol*. 1997;47(1):50-1.
16. Yamashita K, Ishiyama Y, Yoshino M, Tachibana H, Toki D, Konda R, et al. Urinary Tract Infection in Hemodialysis-Dependent End-Stage Renal Disease Patients. *Res Rep Urol*. 2022;14:7-15.
17. Issakhanian L, Behzadi P. Antimicrobial Agents and Urinary Tract Infections. *Curr Pharm Des*. 2019;25(12):1409-23.
18. Richa C, Bhushan CS, Kumar SP, Dev PN, Nabaraj P.Bacteriology of Urinary Tract Infection of Chronic Renal Failure Patients Undergoing for Hemodialysis. J Microbiol Exp,2016, 3(3): 00089.
19. Kwon YE, Oh DJ, Kim MJ, Choi HM. Prevalence and Clinical Characteristics of Asymptomatic Pyuria in Chronic Kidney Disease. *Ann Lab Med*. 2020;40(3):238-44.
20. Kuo IC, Lee JJ, Hwang DY, Lim LM, Lin HY, Hwang SJ,et al. Pyuria, urinary tract infection and renal outcome in patients with chronic kidney disease stage 3-5. *Sci Rep*. 2020;10(1):19460.
21. Dalrymple LS, Go AS. Epidemiology of acute infections among patients with chronic kidney disease. *Clin J Am Soc Nephrol*. 2008;3(5):1487-93.
22. Gilbert DN. Urinary tract infections in patients with chronic renal insufficiency. *Clin J Am Soc Nephrol*. 2006;1(2):327-31.
23. Ozdem S, Bayraktar T, Oktay C, Sari R, Gültekin M. The prevalence of asymptomatic pyuria in diabetic patients: comparison of the Sysmex UF-100 automated urinalysis analyzer with Fuchs-Rosenthal hemacytometer. *Clin Biochem*. 2006;39(9):873-8.
24. Taweel I, Beatty N, Duarte A, Nix D, Matthias K, Al Mohajer M. Significance of bacteriuria in patients with end-stage renal disease on hemodialysis. *Avicenna J Med*. 2018;8(2):51-4.
25. El Nekidy WS, Soong D, Mooty M, Ghazi IM. Treatment of recurrent urinary tract infections in anuric hemodialysis patient, do we really need antimicrobial urinary concentration?. *IDCases*. 2020;20:e00748.

Citation

M. Nawara, A., Abdulsaboor, A., Ahmed, A., Hussein, H. Asymptomatic Urinary Tract Infections in Patients with End Stage Renal Disease on Regular Hemodialysis. *Zagazig University Medical Journal*, 2024; (3795-3808): -. doi: 10.21608/zumj.2024.266665.3148