

“Causative Organism of Acute Pyelonephritis (APN) and Their Antibacterial Susceptibility Pattern- A Study in Rajshahi Medical College Hospital, Rajshahi, Bangladesh”

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ABSTRACT: Introduction: Acute pyelonephritis (APN) is a serious form of urinary tract infection (UTI). Its annual incidence is 250,000 cases in the US and the incidence of hospitalized APN is 11.7 cases per 10,000 population among females and 2.4 cases per 10,000 population among males. The epidemiology of acute pyelonephritis (APN) has changed with time. **Objective:** To find out the Causative Organism of Acute Pyelonephritis (APN) And Their Antibacterial Susceptibility Pattern-A Study In Rajshahi Medical College Hospital, Rajshahi, Bangladesh. **Materials And Methods:** A cross sectional type of observational study on 99 patients who were admitted to Rajshahi Medical College Hospital, Rajshahi, Bangladesh under the diagnosis of APN from January 2019 to Jun 2020, we retrospectively examined clinical symptoms, causes, causative microorganisms, antibiotic sensitivities, and curative urological procedures by reviewing their medical records. All patients with APN (evidenced by history of loin pain, fever and tenderness over the kidneys cost vertebral angle) admitted to department of nephrology of Medical College Hospital will be studied. **Results:** Among total 99 cases, male was 52 cases, female were 47 cases, and the ratio of male to female was 1.9:2. The mean age was 48.48 ± 12.58yr, male was 49.0±19.2 yr., female was 45.0±17.5 yr., and a difference between genders was not detected (p>0.05). In age group of over 60 Yrs. was 14.0%, and highest 34% of over 50Yrs. Duration of hypertension (years) 8.00 ± 3.61, Hospital stay (days) 5.69 ± 0.96, HB% (gm/dl) 10.54 ± 1.26, Total count of WBC (/cmm) 15603.03 ± 3283.68, Neutrophil (%)78.74 ± 3.89, Lymphocyte (%)14.93 ± 5.49, Serum creatinine (mg/dl) 4.59 ± 4.76, RBS (mg/dl) 10.09 ± 6.79, and Total sensitive antibiotic 4.56 ± 2.26, Total

resistant antibiotic 8.89 ± 2.56 respectively. In both males and females, E. coli was the major causative bacteria (82.7% vs. 85.1%), and the portion of Pseudomonas aeruginosa was higher in males than in females (9.6% vs. 8.5%). The cases that bacteria were isolated by blood culture were 99 patients. Similarly, E. coli was detected to be high, 83.0%, followed by the order of Klebsiella pneumoniae, Pseudomonas aeruginosa, and Staphylococcus aureus. Shows in Investigations of APN the AKI was 81.6%, the CKD was 18.4%, both renal failure was 88.9%, and a statistic difference between genders was not detected. The antibiotic sensitivity test of E. coli were 1 (1.2), 3 (4.0), 9 (12.5), 5 (7.1), 63 (86.3), 53 (93.0), 17 (40.5), 16 (26.7), 2 (5.0), 0 (0), 10 (71.4), 10 (71.4), 6 (7.4), 32 (47.8), 18 (22.8), 20 (27.8), 21 (39.6), 42 (56.8), 36 (70.6), 15 (93.8) and 5 (19.2) to Ceftriaxone, Cefixime, Ceftazidime, Cefepime, Imipenem, Meropenem, Azithromycin, Co-trimoxazole, Moxifloxacin, Linezolid, Tigecycline, Cefuroxime, Gentamycin, Gentamycin, Levofloxacin, Doxycycline, Nitrofurantoin, Amikacin, Piperacilin-tazobactam, Co-Amoxyclave. In comparison with E. coli, and pneumoniae was found to be more susceptible to Ceftriaxone /Tigecycline. Significantly resistant (p<0.05). **Conclusion:** In addition, in APN, sepsis is associated in 11.45%, and resistance to antibiotics shows a trend on the rise, hence, clinical attentions are required. Particularly, antibiotics resistance to ampicillin and Ceftriaxone /Tigecycline is high and the sensitivity is on the decrease with the time, therefore, it is thought that the reconsideration of their selection as first-line drugs is required.

Key Words: Urinary Tract Infections; Pyelonephritis; Urologic Surgical Procedures.

I INTRODUCTION

Acute pyelonephritis (APN) is a serious form of urinary tract infection (UTI). Its annual incidence is 250,000 cases in the US and the incidence of hospitalized APN is 11.7 cases per 10,000 population among females and 2.4 cases per 10,000 population among males [1]. Urinary tract infection (UTI) is one of the most common bacterial infections seen in developing countries like Bangladesh. As many as 50-80% of women in the general population acquire at least one UTI during their life time and about 20-30% of women who have had one episode of UTI will have recurrent episodes. This study is, therefore, designed to determine the bacterial uropathogens and their antibiotic resistance pattern among patients with complaints of UTIs in Dhaka city. While in Korea, the incidence rate is 35.7 cases per 10,000 population [2]. Clinical manifestations include severe systemic symptoms such as high fever, chilling, nausea and vomiting. Without proper treatments, the renal pelvis and its parenchyme can be damaged, possible following sepsis that may lead to death. In the cases with associated sepsis, the mortality reaches 10-20% [3, 4]. In South Asia, Korea, Africa the high mortality (2.1 cases per 1,000 persons among hospitalized patients) has been reported [2]. Key consideration in the treatment of APN is to understand the current characteristics of the current community, causative bacterial spectrum, and antibiotic resistance patterns. Antibiotic resistance is on the gradual increase, and ampicillin and trimethoprim/sulfamethoxazole (TMP/SMX) that have been the first-line antibiotics could not show effective sensitivity any longer [5]. And at the early phase of the treatment for APN when the isolation of causative microorganisms is not performed yet, antibiotics should be administered empirically. It is required to understand accurately the presently most frequent causative microorganisms and antibiotic resistance. In addition, as the westernized life style and eating habit are accelerating prevalence of diabetes and other chronic diseases as well as Bangladesh society is getting more aged, the alteration of the epidemiology of APN is anticipated, with its epidemic examination at regular basis. The cases with underlying causes are referred to as complicated APN, and its proportion is 21.1-37.8% [1-4]. Although APN could be treated readily with appropriate antibiotics, hydration, and bed rest,

complicated APN should be done with correcting its cause. Moreover, it has been reported that complicated APN shows high positive rate with blood culture and more severe clinical symptoms than those of simple APN [5, 6]. Therefore, we examined the current clinical characteristics and the necessity of surgical treatment in 80 cases of APN patients for the past one half years.

II OBJECTIVES

General objective:

1. To identify causative bacteria and their antibacterial susceptibility pattern in patients with APN.

Specific objectives:

1. To see the socio-demographic profile of the patients with APN.
2. Other risk factors associated with development of APN.

III MATERIALS AND METHODS

A cross sectional type of observational study on 99 patients who were admitted to Rajshahi Medical College Hospital, Rajshahi, Bangladesh under the diagnosis of APN from January 2019 to Jun 2020, we retrospectively examined clinical symptoms, causes, causative microorganisms, antibiotic sensitivities, and curative urological procedures by reviewing their medical records. All patients with APN (evidenced by history of loin pain, fever and tenderness over the kidneys cost vertebral angle) admitted to department of nephrology of Medical College Hospital will be studied. In addition to the clinical diagnosis, patients were required to meet more than 3 of the following 5 criteria: 1) clinical symptoms of APN (chilling, nausea, vomiting, flank pain); 2) cost vertebral angle tenderness; 3) leukocytosis (higher than 10,000/ μ L); 4) fever (higher than 38.5°C); 5) white blood cell (WBC) count \geq 5 cells per high power field on centrifuged urine sediment or more 100,000 CFU/mL microorganisms in urine culture (7). Infected site (right, left, and both) was localized with clinical symptoms such as flank pain and cost vertebral angle tenderness. In cases which clinical symptoms were vague, we judged the localization by radiologic findings. The urine collecting methods for males were that lift the prepuce, wash the urethral meatus with 2% boric sponge, and collect the mid-stream urine in a sterile plastic cup with a lid, and in female cases, in the lithotomy position, wash the perineum and the urethral meatus by the identical method, and collect the mid-stream urine was using a nelaton catheter.

Inclusion criteria:

1. Patients of all age clinically diagnosed cases of APN will be included in this study.
2. Both male and female will be included.

Exclusion criteria:

1. Patients with history of recent (probable duration if significant) urinary tract procedure.
2. Patients with urinary tract injuries.

Data collection: After clinical diagnosis, patients who will meet inclusion and exclusion criteria will be selected in the study. After selection history regarding age, sex, presence and duration of diabetes and hypertension will be recorded. Full blood count, serum creatinine, urea, blood sugar and urine examination for albumin, sugar, RBC and WBC will be done. Ultrasonography of abdomen and plain X-ray KUB will be done to identify any urinary tract pathology. For urine culture patients will be advised to collect a clean catch midstream urine sample in a sterile wide mouthed container supplied by laboratory and to bring the sample to laboratory as early as possible. Identification of bacterial pathogens will be done by microscopy, culture and conventional biochemical tests. Antibiotic susceptibility testing will be done for ceftriaxone, cefixime, ceftazidime, cefepime, imipenem, meropenem, azithromycin, cotrimoxazole, moxifloxacin, linezolid, tigecycline, cefuroxime, gentamycin, ciprofloxacin, levofloxacin, doxycycline, nitrofurantoin, amikacin, piperacillin-tazobactam and coamoxyclav. Presence of renal failure need for dialysis and hospital stay will be recorded as outcome variable. The collected urine was inoculated to blood agar broth and MacConkey broth, 0.001 mL each, cultured in a 37°C incubator for 24 hr, and the number of bacterial colony per 1 mL urine was calculated. The blood was also inoculated to blood agar broth and MacConkey broth, cultured for 5 days, and the growth of bacteria was assessed.

The identification of bacteria and antibiotic sensitivity were assessed by the disk diffusion test described by the National Committee for Clinical Laboratory Standards. Clinical symptoms, sign, and the presence of lower urinary tract symptoms were assessed, and the duration of the fever higher than 38.5°C, the duration of the flank pain, and the duration of the costovertebral angle tenderness were assessed. To diagnosis

complicated APN, we examined the presence of following diseases: structural and functional abnormalities (urinary tract stone disease, neurogenic bladder, vesicoureteral reflux (VUR), obstructive uropathy, prostate disease); urologic manipulation (cystoscopic or ureteroscopic examination, indwelling catheter, kidney transplantation); the underlying diseases which contribute to the persistence of infection or suppression of immune system (diabetes, immunosuppressive state, cystic renal disease).

Data Analysis: As statistics, comparison of continuous variables between independent two groups was performed by t-test, comparison of the frequency was analyzed by Pearson chi-square test, and the criterion of the determination of significance was $p < 0.05$. Antibiotics are the first course of action against acute pyelonephritis. However, the type of antibiotic your doctor chooses depends on whether or not the bacteria can be identified. If not, a broad-spectrum antibiotic is used. Although drugs can cure the infection within 2 to 3 days, the medication must be taken for the entire prescription period (usually 10 to 14 days). In some cases, drug therapy is ineffective. For a severe kidney infection, your doctor may admit you to the hospital. The length of your stay depends on the severity of your condition and how well you respond to treatment. Treatment may include intravenous hydration and antibiotics for 24 to 48 hours. While you're in the hospital, doctors will monitor your blood and urine to track the infection. You'll likely receive 10 to 14 days' worth of oral antibiotics to take after you're released from the hospital.

IV RESULTS

Among total 99 cases, male was 52 cases, female were 47 cases, and the ratio of male to female was 1.9:2. The mean age was 48.48 ± 12.58 yrs., male was 49.0 ± 19.2 yr., female was 45.0 ± 17.5 yr., and a difference between genders was not detected ($p > 0.05$). In age group of over 60 yrs. was 14.0%, and highest 34% of over 50 yrs. Duration of hypertension (years) 8.00 ± 3.61 , Hospital stay (days) 5.69 ± 0.96 , HB% (gm/dl) 10.54 ± 1.26 , Total count of WBC (/cmm) 15603.03 ± 3283.68 , Neutrophil (%) 78.74 ± 3.89 , Lymphocyte (%) 14.93 ± 5.49 , Serum creatinine (mg/dl) 4.59 ± 4.76 , RBS (mg/dl) 10.09 ± 6.79 , and Total sensitive antibiotic 4.56 ± 2.26 , Total resistant antibiotic 8.89 ± 2.56 respectively [Table & Figure-1].

Table-1: Comparison between the clinical features of APN (N=99)

Variables	Mean ± SD
Age (years)	48.48 ± 12.58
Duration of diabetes (years)	7.44 ± 4.09
Duration of hypertension (years)	8.00 ± 3.61
Hospital stay (days)	5.69 ± 0.96
HB% (gm/dl)	10.54 ± 1.26
ESR (mm in 1 st hour)	94.85 ± 19.61
Total count of WBC (/cmm)	15603.03 ± 3283.68
Neutrophil (%)	78.74 ± 3.89
Lymphocyte (%)	14.93 ± 5.49
Serum creatinine (mg/dl)	4.59 ± 4.76
RBS (mg/dl)	10.09 ± 6.79
Total sensitive antibiotic	4.56 ± 2.26
Total resistant antibiotic	8.89 ± 2.56

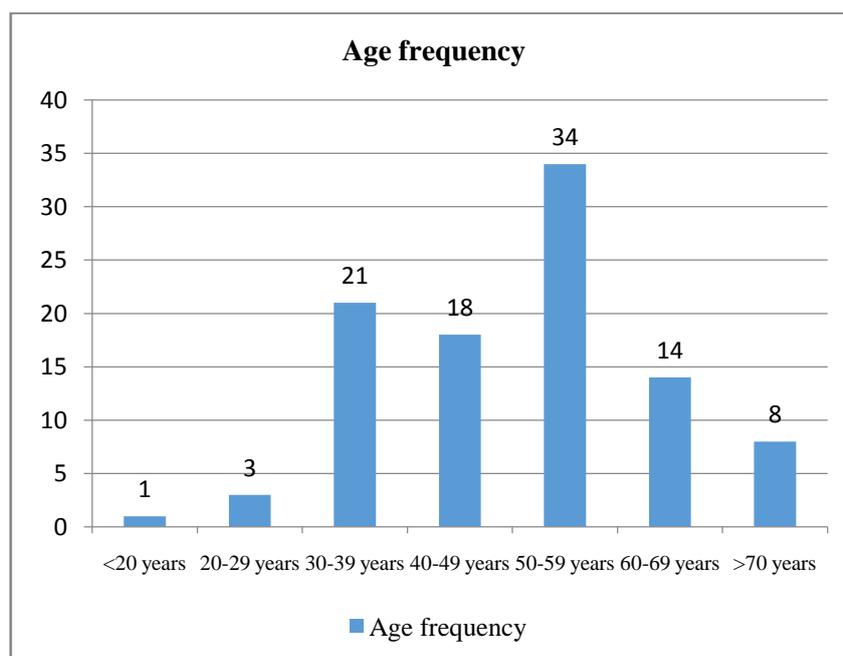


Figure-1: Age distribution of APN patients.

The age group included in this study ranged between 20 to 70years. The maximum numbers of

pregnant women were in the age group of 50-59 years (34.0%) [Figure-2].

Table-2:Sociodemographic characteristics of APN (N=99)

		Frequency	%
Age			
	<30 years	4	4.0
	>30 years	95	96.0
Sex			
	Male	52	52.5
	Female	47	47.5

DM	50	50.5
Duration >10 years	17	34.0
Hypertension	29	29.3
Duration >5 years	26	89.7
Residence		
Urban	25	25.3
Rural	74	74.7
Hospital stay \geq 6 days	53	53.5

The Sociodemographic characteristics of APN patients highest age frequency >30 Yrs. 95(96.0%) and sex male 52(52.5%) and female

47(47.5%), DM 50.5% hypertension highest >5 Yrs. Duration 89.7%, residence urban 25.3% and rural 74.7% [Table-2].

Table-3: Investigations of APN (N=99)

	Frequency	%
Renal failure	88	88.9
AKI	71	81.6
CKD	16	18.4
TC (WBC) >11,000/ cmm	98	99.0
Urine albumin		
+	57	57.6
++	31	31.3
+++	2	2.0
Urine pus cell		
<10	7	7.1
10-20	20	20.2
20-30	8	8.1
>30	64	64.6
Urine RBC		
<5	51	51.5
5-10	39	39.4
10-20	3	3.0
>20	6	6.1
Renal stone	2	2.0
BOO	15	15.2

Table-4: Relationship of types of bacteria isolated from urine culture with clinic pathological characteristics of the subjects (N=99)

	E. coli (n=83) n (%)	Pseudomonas (n=9) n (%)	Klebsiella (n=3) n (%)	Streptococcus/ Staphylococcus	Total

					(n=4) n (%)	
Age	<30	4 (100.0)	0 (0)	0 (0)	0 (0)	4
	>30	79 (83.2)	9 (9.5)	3 (3.2)	4 (4.3)	95
Sex	Male	43 (82.7)	5 (9.6)	1 (1.9)	3 (5.7)	52
	Female	40 (85.1)	4 (8.5)	2 (4.3)	1 (2.1)	47
DM		41 (82.0)	4 (8.0)	2 (4.0)	3 (6.0)	50
	Duration >10 years	15 (88.2)	1 (5.9)	1 (5.9)	0 (0)	17
Hypertension		24 (82.8)	3 (10.3)	1 (3.4)	1 (3.4)	29
	Duration >5 years	23 (88.5)*	2 (7.7)	1 (3.8)	0 (0)**	26
Renal failure		72 (81.8)	9 (10.2)	3 (3.4)	4 (4.5)	88
	AKI	61 (85.9)	6 (8.5)	1 (1.4)	3 (4.2)	71
	CKD	11 (68.8)	2 (12.5)	2 (12.5)*	1 (6.2)	16
	*p<0.05, **p<0.01					

Shows in Investigations of APN the AKI was 81.6%, the CKD was 18.4%, both renal failure was 88.9%, and a statistic difference between genders was not detected. The duration of fever, the duration of the flank pain, and the duration of the costovertebral angle tenderness was 3.1 days, 3.7 days, and 4.2 days, respectively [Table-3].

In complicated APN, the duration of the flank pain and the cost vertebral angle tenderness was statistically significantly longer than in simple APN and the portion of male against female (F:M=1.9:2.1) was higher than that of simple APN (1.1:1). However, age, duration of fever, and urine culture positive rate between genders were not different, respectively [Table-4]. In both males and females, E. coli was the major causative bacteria (82.7% vs. 85.1%), and the portion of

Pseudomonas aeruginosa was higher in males than in females (9.6% vs. 8.5%). The cases that bacteria were isolated by blood culture were 99 patients. Similarly, E. coli was detected to be high, 83.0%, followed by the order of Klebsiella pneumoniae, Pseudomonas aeruginosa, and Staphylococcus aureus [Table-4]. But each infection has no difference against the rate of sepsis in this study. In the cases that microorganisms were isolated in the blood culture, the duration of the flank pain was significantly longer than negative cases (5.69 ± 0.96 days) ($p < 0.05$). None of the duration of fever, the duration of the flank pain, the duration of the costovertebral angle tenderness according to the isolated microorganisms were statistically different ($p > 0.05$).

Table-5: Susceptibility of bacteria to various drugs (N=99)

Antibiotic	E. coli (n=83) n (%)	Pseudomonas (n=9) n (%)	Klebsiella (n=3) n (%)	Streptococcus/ Staphylococcus (n=4) n (%)	Total
Ceftriaxone	1 (1.2)****	1 (16.7)***	1 (33.3)****	0 (0)	3 (3.1)
Cefixime	3 (4.0)	0 (0)	0 (0)	0 (0)	3 (3.5)
Ceftazidime	9 (12.5)	4 (44.4)**	0 (0)	0 (0)	13 (14.8)
Cefepime	5 (7.1)*	4 (44.4)**	0 (0)	0 (0)	9 (10.3)
Imipenem	63 (86.3)	7 (100)	1 (100)	2 (50.0)***	73 (85.9)
Meropenem	53 (93.0)	5 (83.3)	3 (100)	2 (66.7)	63 (91.3)
Azithromycin	17 (40.5)	1 (33.3)	0 (0)	0 (0)	18 (37.5)
Co-trimoxazole	16 (26.7)	0 (0)	1 (50.0)	0 (0)	17 (23.3)
Moxifloxacin	2 (5.0)	0 (0)	0 (0)	0 (0)	2 (4.1)

Linezolid	0 (0)	0 (0)	0 (0)	1 (50.0)*	1 (8.3)
Tigecycline	10 (71.4)*	0 (0)***	0 (0)	0 (0)	10 (55.6)
Cefuroxime	6 (7.4)	0 (0)	0 (0)	0 (0)	6 (6.4)
Gentamycin	32 (47.8)	4 (44.4)	1 (33.3)	2 (66.7)	39 (47.6)
Gentamycin	18 (22.8)*	6 (66.7)**	1 (33.3)	0 (0)	25 (26.0)
Levofloxacin	20 (27.8)	5 (62.5)*	2 (66.7)	0 (0)	27 (31.4)
Doxycycline	21 (39.6)	0 (0)	0 (0)	2 (66.7)	23 (39.7)
Nitrofurantoin	42 (56.8)	4 (66.7)	2 (66.7)	1 (33.3)	49 (57.0)
Amikacin	36 (70.6)	5 (83.3)	2 (66.7)	1 (33.3)	44 (69.8)
Piperacilin-tazobactam	15 (93.8)	3 (100)	0 (0)	1 (50.0)***	19 (90.5)
Co-Amoxyclove	5 (19.2)	1 (33.3)	0 (0)	1 (33.3)	7 (20.6)
Total	72 (82.8)	8 (9.2)	3 (3.4)	4 (4.5)	

*- Significantly susceptible (p<0.05), **- Significantly susceptible (p<0.01), ***- Significantly resistant (p<0.05), ****- Significantly resistant (p<0.01).

E. coli was most commonly sensitive to Meropenem (93.0%) and Nitrofurantoin (56.8%), Klebsiella and staphylococcus aureus were sensitive to cephalosporins and ciprofloxacin (85.7%). Klebsiella were most commonly sensitive to Imipenem (100%) and Meropenem (100%). The antibiotic sensitivity test of E. coli were 1 (1.2), 3 (4.0), 9 (12.5), 5 (7.1), 63 (86.3), 53 (93.0), 17 (40.5), 16 (26.7), 2 (5.0), 0 (0), 10 (71.4), 10 (71.4), 6 (7.4), 32 (47.8), 18 (22.8), 20 (27.8), 21 (39.6), 42 (56.8), 36 (70.6), 15 (93.8) and 5 (19.2) to Ceftriaxone, Cefixime, Ceftazidime, Cefepime, Imipenem, Meropenem, Azithromycin, Cotrimoxazole, Moxifloxacin, Linezolid, Tigecycline, Cefuroxime, Gentamycin, Gentamycin, Levofloxacin, Doxycycline, Nitrofurantoin, Amikacin, Piperacilin-tazobactam, Co-Amoxyclove. On the other hand, the mean rates of sensitivity of Pseudomonas were 1 (16.7), 0 (0), 4 (44.4), 4 (44.4), 7 (100), 5 (83.3), 1 (33.3), 0 (0), 0 (0), 0 (0), 0 (0), 4 (44.4), 6 (66.7), 5 (62.5), 0 (0), 4 (66.7), 5 (83.3), 3 (100), 1 (33.3). Klebsiella 0 (0), 3 (3.2), 1 (1.9), 2 (4.3), 2 (4.0), 1 (5.9), 1 (3.4), 1 (3.8), 3 (3.4) and 1 (1.4). Streptococcus/ Staphylococcus, 0 (0), 4 (4.3), 3 (5.7), 1 (2.1), 3 (6.0), 0 (0), 1 (3.4), 0 (0), 4 (4.5), 3 (4.2). In comparison with E. coli, and pneumoniae was found to be more susceptible to Ceftriaxone/Tigecycline Significantly resistant (p<0.05) [Table-5].

V DISCUSSION

UTI is bacterial infection that can be encountered frequently in clinics, and APN is the most severe form of UTI. Depending on reports, the ratio of male to female varies from 1:7 to 1:13.1 [8-10], and in our study, similarly, it was 1:7.7, and found to be substantially more prevalent in females. Emphysematous pyelonephritis is an uncommon and severe form of necrotizing infection of renal parenchyma and collecting system characterized by gas formation. Patients with diabetes mellitus are the usual sufferers and rarely an episode of emphysematous pyelonephritis may unmask previously undiagnosed diabetes [31]. Here we report a case of class IV emphysematous pyelonephritis [32], occurring in a middle aged Bangladeshi females. Numerous studies have been reported that in young women who are sexually active, and using a diaphragm or spermicide recurrent UTI could occur [11]. In addition, in our study, the proportion of female cases older than 60 yr is 23.7%, which is higher than previous studies reported in Bangladesh [32]. It is considered that the reasons of low rates of the positive culture rate in such manners are that many patients have taken antibiotics without prescription and while being treated at private clinics previously, with antibiotics as well. As for causative microorganisms, E. coli accounted for 84.3%, and in agreement with previous reports, which turned out markedly prevalent [8-10]. Among isolated microorganisms,

the important point to which attentions have to be paid is that only in the cases with risk factors such as neurogenic bladder, kidney transplantation, urethral stricture, Pseudomonas was cultured, and males were 80%, which was prevalent. In our study, the antibiotic sensitivity test for ampicillin to E. coli to was 1 (1.2), 3 (4.0), 9 (12.5), 5 (7.1), 63 (86.3), 53 (93.0), 17 (40.5), 16 (26.7), 2 (5.0), 0 (0), 10 (71.4), 10 (71.4), 6 (7.4), 32 (47.8), 18 (22.8), 20 (27.8), 21 (39.6), 42 (56.8), 36 (70.6), 15 (93.8) and 5 (19.2) to Ceftriaxone, Cefixime, Ceftazidime, Cefepime, Imipenem, Meropenem, Azithromycin, Co-trimoxazole, Moxifloxacin, Linezolid, Tigecycline, Cefuroxime, Gentamycin, Gentamycin, Levofloxacin, Doxycycline, Nitrofurantoin, Amikacin, Piperacilin-tazobactam, Co-Amoxyclave. On the other hand, the mean rates of sensitivity of Pseudomonas were 1 (16.7), 0 (0), 4 (44.4), 4 (44.4), 7 (100), 5 (83.3), 1 (33.3), 0 (0), 0 (0), 0 (0), 0 (0), 4 (44.4), 6 (66.7), 5 (62.5), 0 (0), 4 (66.7), 5 (83.3), 3 (100), 1 (33.3). Klebsiella 0 (0), 3 (3.2), 1 (1.9), 2 (4.3), 2 (4.0), 1 (5.9), 1 (3.4), 1 (3.8), 3 (3.4) and 1 (1.4). Streptococcus/Staphylococcus, 0 (0), 4 (4.3), 3 (5.7), 1 (2.1), 3 (6.0), 0 (0), 1 (3.4), 0 (0), 4 (4.5), 3 (4.2). In comparison with E. coli, and pneumoniae was found to be more susceptible to Ceftriaxone/Tigecycline Significantly resistant ($p < 0.05$). The second most common bacterial infection in human population is urinary tract infection (UTI). It is also one of the most frequently occurring nosocomial infections [33]. The annual global incidence of UTI is almost 250 million. Approximately 35% of all hospital acquired infections are contributed by UTI [33,34]. It is the most common bacterial infection ranging from asymptomatic to severe sepsis. Acute pyelonephritis (APN) is an infection of the upper urinary tract, especially the renal parenchyma and renal pelvis. Misdiagnosis may lead to sepsis, renal abscess and chronic pyelonephritis that may cause secondary hypertension and renal failure. APN occurs in at least 250000 adults per year in the United States [35]. It is the most severe form of UTI [36,37]. It often requires hospitalization and prolonged therapy and when accompanied by bacteremia, APN has a mortality rate of 10% to 20% [38,39,40]. In acute infection E. coli is the most frequent infecting organism. But the prevalence of the antibiotic resistant organisms such as klebsiella, proteus, serratia, enterobacter, Pseudomonas increases in complicated UTI's. Among gram positive bacteria S. saprophyticus, E. faecalis, S. agalactiae, S. pyogenes, S. aureus are

usually present and resistant to variety of antibiotics [41,42]. The rate of antibiotic resistance is high among uropathogens. Frequency of resistance to antibiotic directly linked to irrational use of antibiotics and use of antibiotic used in inadequate dose and duration. Treatment of UTI is often started empirically and therapy is based on information determined from the antimicrobial sensitivity pattern of the urinary tract pathogens in a given community [43, 44]. Now a day's more and more drug resistant strains of uropathogens have been isolated in patients with APN admitted to hospital than before. Ongoing research on susceptibility pattern of uropathogens is necessary for precise choice of empirical antibiotic.

In other countries, it has been reported that antibiotic sensitivity for TMP/SMX was 67-83.2%, 78-98.1% for ciprofloxacin and 25-82.3% for ampicillin [12-14]. In South Asia, according to Min et. Al. they have reported that antibiotic sensitivity for ampicillin was 13.2%, to TMP/SMX 44.7%, to ciprofloxacin 86.5%, and to amikacin 98.3% [10]. According to our study and previous studies reported in Bangladesh, we found that the antibiotic resistance of ampicillin and TMP/SMX is higher than that of western countries [10]. In the cases associated with sepsis, high mortality and save clinical symptoms were accompanied [3, 4]. In our study, similarly, in the cases that bacteria were isolated in blood culture, the duration of flank pain was significantly longer than other cases. In contrary Nitrofurantoin resistance of E.coli which was observed by Akram et al. [27], from Aligarh, India in 2006 has changed in our study in 2015 where we observed high sensitivity of E.coli against Nitrofurantoin. This may be due to less use of Nitrofurantoin during this period has revived the sensitivity. High sensitivity of E.coli for fluoroquinolones as observed by Shalini et al [28], has now changed as evident in our study and other studies by Durgesh et al. [29], and Rijal et al. [30]. In mild APN, Infectious Diseases Society of America (IDSA) recommends an oral fluoroquinolone for empirical therapy. If the organism is known to be susceptible, oral TMP/SMX provides an alternative [15]. If a patient at the time of presentation is sufficiently ill to require hospitalization (high fever, high white blood cell count, vomiting, dehydration, or evidence of sepsis) or fails to improve during an initial outpatient treatment period, intravenous fluoroquinolone, an aminoglycoside with or without ampicillin, or an extend-spectrum cephalosporin with or without an aminoglycoside

are recommended [15]. Concerning the duration of treatment, the regimen of intravenous injection for 7 days and subsequently oral administration for 1 week or 2 weeks are recommended [16]. In addition, Talan et al. [17] recommended the regimen of oral fluoroquinolone for 7 days or TMP/SMX for 14 days. Finkelstein et al. [18] have reported that in complicated APN, the longer time was required for the amelioration of clinical symptoms, and such result was validated in our study. More specific medical or surgical therapy and urinary tract drainage may be required when necessary [19]. Most of the complicated APN patients who didn't receive surgical treatment were DM patients. And the others were the diseases that were impossible to operate (e.g., nephrocalcinosis, medullary sponge kidney, polycystic kidney), spontaneous expelled urinary stone disease, low-grade VUR, voiding dysfunction managed by medical therapy (alpha adrenergic blocking agents, anticholinergics, or cholinergic agents), and so on. But physicians should closely follow up these patients to prevent recurrent infection. Factors that may predispose diabetics to complicated infections include autonomic neuropathy leading to poor bladder emptying and urinary stasis, microangiopathy, leukocyte dysfunction, and frequent urinary tract instrumentation [20]. The prevalence of bacteriuria is twice higher than the nondiabetics and asymptomatic bacteriuria in diabetes frequently progresses to symptomatic and upper UTIs, so it should be treated. In addition, APN in DM patients is 5 times more frequent than the nondiabetics [21] and can lead to serious complications like septic shock, EPN, renal and perirenal abscess, and papillary necrosis [22]. Upper urinary tract obstruction, whether primary or secondary, due to infravesical obstruction (e.g. prostatic diseases, neurogenic bladder), can lead to highly elevated intrapelvic pressure allowing

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intrarenal reflux of infected urine. In these patients, instant drainage of the obstruction is mandatory as is the immediate institution of broad-spectrum antimicrobial treatment. If proper therapy is delayed, the infection might progress to pyonephrosis, renal abscess or urosepsis that still has a high mortality [23]. Recommended antibiotic agents are fluoroquinolone, aminopenicillin/beta-lactamase inhibitor, and second-generation cephalosporin. In addition, in the case with an indwelling catheter in the bladder, the possibility of bacteriuria is increased daily by 3-10%, and thus after one month, bacteriuria is detected in most cases [24]. Most cases are asymptomatic, however, sepsis may be associated in less than 5%, and thus if indwelling catheters are required, to prevent the development of bacteriuria, it is required to maintain a closed system, and clinicians should make efforts to remove the catheter as early as possible [25, 26].

VI CONCLUSION

In addition, in APN, sepsis is associated in 11.45%, and resistance to antibiotics shows a trend on the rise, hence, clinical attentions are required. Particularly, antibiotics resistance to ampicillin and Ceftriaxone /Tigecycline is high and the sensitivity is on the decrease with the time, therefore, it is thought that the reconsideration of their selection as first-line drugs is required.

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