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ORIGINAL ARTICLE

RECURRENT URINARY TRACT INFECTION- ETIOLOGY, RISK FACTORS AND OUTCOME IN A TERTIARY CARE HOSPITAL OF BANGLADESH

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Abstract:

Background: *Urinary tract infections (UTIs) are one of the major causes of morbidity and comorbidities in patients with underlying conditions, and it accounts for the majority of the reasons for hospital visit globally. The high prevalence of recurrent UTIs represents a modifiable determinant for both societal and personal burdens and is associated with a significant burden of morbidity and mortality in the elderly, among whom UTIs are most prevalent. The aim of the study was recurrent urinary tract infection- etiology, risk factors and outcome.* ***Methods:*** *This cross-sectional descriptive type of observational study was conducted in the Department of Nephrology in Anwer Khan Modern Medical College Hospital, Dhaka, Bangladesh from January 2023, to December 2023. A total no of 93 patients were included in the study. Inpatients, age range 21-85 years, presenting or highly suspicious of having UTIs and the occurrence of e"2 symptomatic episodes within 6 months or e"3symptomatic episodes within 12 months were recruited in the study. Any patient who was terminally ill, who fails to give urine samples, with a history of antibiotic administration in the last two weeks and any female who was in their menstruation period were excluded from the study.* ***Results:*** *Among them 79 were female and 14 were male. Female to male ratio was 5.64:1. Mean age of the patients was 58.61±17.51 (Mean±SD). Most of the patients were of 61-70 years age group 23/93 (24.73%) and after that41-50 years 19/93 (20.43%). 92.47% (86/93) were married and 7.53% (7/93) were unmarried. Most of the patients were of Diabetes mellitus (DM) 57/93 (61.29%). After that Hypertension, Chronic Kidney Disease (CKD) and CKD + DM about 51/93 (54.84%), 39/93 (41.94%) and 36/93 (38.71%) respectively. 54/79 (68.35%) were of menopause and 24/79 (30.38%) women had regular menstrual cycle. 1/79 (1.27%) was pregnant. Escherichia coli(E coli) was the most prevalent uropathogens with 47/93 (50.54%) followed by Klebsiella pneumoniae 12/93 (12.90%), Pseudomonas aeruginosa 10/93 (10.75%), Streptococcus pyogenes 8/93 (8.60%), Staphylococcus aureus 6/43 (6.45%), Enterococcus faecalis 5/93 (5.38%) and others 5/93 (5.38%). 77.42% were of relapse and 22.52% were of reinfection. The Mean±SD of HbA1c was 7.83±2.15% and that of Serum creatinine and Hemoglobin were 2.17±1.18 mg/dl and 9.82±2.60gm%. On routine examination of urine, 39/93 (41.94%) patient had trace albumin present in urine and 57/93 (61.29%) had reducing sugar. 71/93 (76.34%) had1-2 pus cell in urine and 22/93 (23.66%) presented with plenty of pus cell with 19/93 (20.43%) had 0-4 RBC's (Red blood cell). Factors associated with recurrent UTI were Age >50 years (56.99%), Female gender (84.95%), Married (92.47%), Menopause (58.06%), Diabetes mellitus (61.29%), Indwelling catheter >6 days (25.81%) and Genitourinary abnormalities (15.05%).* ***Conclusion:*** *This study has demonstrated that hospitalization, married individuals, duration of catheter, diabetes mellitus, genitourinary tract abnormalities, female gender and menopause are the most important factors associated with UTIs. Appropriate measures may help to reduce UTIs due to these associated factors. We recommend routine UTIs screening of patients of the following category: hospitalized, genitourinary tract abnormalities, indwelling catheter, diabetic, female gender, menopause and married individuals. If these routine checks are put in place, prevention of UTI can be realized at lower cost.*

Key words: *Recurrent UTI, Menopause, Diabetes mellitus, CKD*

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Introduction:

Urinary tract infections (UTIs) are one of the major causes of morbidity and comorbidities in patients with underlying conditions, and it accounts for the majority of the reasons for hospital visit globally[1]. Urinary tract infections (UTIs) are the most common outpatient infections, with a lifetime incidence of 50"60% in adult women[2].

The burden of recurrent UTIs has both personal and societal aspects. The societal burden includes the clinical and economic burden of the illness, and the personal burden includes social and psychological effects which have a negative impact on quality of life (QoL). The high prevalence of recurrent UTIs represents a modifiable determinant for both societal and personal burdens, hence the importance of disease prophylaxis. Consultations for UTIs represent between 1% and 6% of all medical visits (~7 million visits and ~US$1.6 billion annually). They are associated with a significant burden of morbidity and mortality in the elderly, among whom UTIs are most prevalent[3,4].

Recurrent UTIs are associated with symptoms of anxiety and depression. The sudden, rapid, and painful onset of a UTI is often a source of anxiety in patients. Feelings of guilt related to a patient's inability to perform their usual activities, or the impact of recurrent infections on their social activities, may lead to clinical symptoms of depression. The social impact of recurrent UTIs may be particularly marked in premenopausal, working women. Treatment of a UTI alone is often not enough to improve a patient's QoL. However, the often-neglected impact of therapy on QoL should be considered as part of treatment efficacy. In the elderly, the potential for a substantial impact on general health, including issues such as incontinence, is also associated with a significant psychological burden[5].

The personal and societal impacts of recurrent UTIs often overlap. For example, in cases where multiple urine cultures or imaging studies may be required, the diagnostic burden both affects QoL and has a substantial negative economic impact. Costs may be both direct and indirect: work absenteeism, for example, can impact both the economy and a patient's sense of wellbeing. Costs include those associated with medical visits (for ambulatory patients), prescriptions for antimicrobials, hospital expenses, nonmedical travel-related costs, days of sick leave due to the disease, and the treatment of related comorbidities[2].

The recent multinational web-based GESPRIT study assessed both the personal and economic burden of recurrent UTIs in Europe (Germany, Switzerland, Poland, Russia, and Italy). Adult women (~*18 years of age) with a history of recurrent infection and who currently had an acute infection (n = 1275) or had suffered an infection within the previous 4 weeks (n = 666) completed an online questionnaire. Recurrent UTIs were associated with an economic burden due to both sick leave and physician visits. Participants also reported a significant impact on QoL as evaluated by the SF-12 v2 health survey. The majority of women surveyed (approximately 80%) reported having received treatment with antibiotics. Prophylaxis was frequently delayed beyond the point where recurrence was established (~*3 UTIs in 12 months), and the behavioral measures used for prophylaxis were often ineffective[6].

Methods:

This study was conducted in the Department of Nephrology in Anwer Khan Modern Medical College Hospital, Dhaka, Bangladesh.The sample size of 93 depending upon the availability of the patient during the study period. This was a cross-sectional descriptive type of observational studyconducted from January 2023, to December 2023. Inpatients, age range 21-85 years, presenting or highly suspicious of having UTIsand occurrence of e”2 symptomatic episodes within 6 months or e”3symptomatic episodes within 12 months were recruited in the study. Any patient who was terminally ill, who fails to give urine samples, with a history of antibiotic administration in the last two weeks and any female whowas in their menstruation period were excluded from the study. Simple random sampling technique was applied to recruit patients who have satisfied the selection criteria from each hospital's inpatient departments. Then, questionnaires with both open-ended questions such as age and closed ended questions with nominal categorical values such as gender were administered. Data including age, gender, tribe, residence, level of education, and history of medical conditions were collected by clinicians. Capillary blood and midstream urine (MSU) samples were collected after obtaining informed consent from the selected patients. Capillary blood was used for screening of selected factors associated with UTIs such as diabetic test, and only female patients aged 21-45 underwent additional rapid pregnancy test and the results were recorded accordingly.

In this test, one strip was used per individual. The patient's identification number was labeled on the test strip. The test strip was dosed with 2.5 microliters of whole blood. The test result was read using an optium glucometer and recorded in 20 seconds. The normal standard reference ranges are random blood sugar (RBS) (3.3–7.4 mmol/l) or fasting blood sugar (FBS) (3.6 6.4 mmol/l) for adults. Diabetic mellitus diagnostic

values when using capillary whole blood were follows: FBS ise"6.7mmol/l, and RBS ise"11.1mmol/l (Abbot Diabetes Care Ltd., UK).

A human chorionic gonadotropin (HCG) test was used to detect the presence of HCG hormones in females' age e"21 years. The levels of HCG were detected using the early pregnancy test and ovulation predictors kits: FAQ (ACON Laboratories, Inc., USA). In this test, one strip was used per individual. The patient's identification number was labeled on the test strip. The test strip was dipped into a bottle of urine. Within 5 minutes, the result was read. Positive result: color bands appeared on both the test and control regions. Negative result: no color band appeared onthetestregion, anda colorbandappearedinthe control region.

A "clean catch" midstream urine sample was collected in sterile clean leak proof bottles from each patient. To avoid contamination of the specimen, all participants were required to first cleanse the urethral area with a castile soap towelette (Professional Disposables International, Inc., Canada). In addition, female participants were required to wide open the labia apart before sample collection. The MSU was then collected into a wide mouth clean sterile urine container. In patients with urinary catheters, urine specimens were collected from fresh catheters using a syringe and then transferred to a sterile specimen tube.

Isolation and identification of the bacterial uro-pathogens was done microbiology laboratory. Each sample of the uncentrifuged, uniformly mixed MSU samples was inoculated on Cystine Lactose Electrolyte Deficient Agar (CLED) and incubated at 37°C aerobically for 24hrs[7]. After incubation, the cultures were subcultured on MacConkey agar and Sheep Blood Agar (BA) media, observed, and recorded. Positive UTI was recorded after having presence of 100,000 colony-forming units (CFU) per milliliter in the culture of an appropriate collected MSU[8]. The isolates observed on the selective media were preserved in 40% glycerol at "80°C. For Gram-negative bacteria, standard identification procedures of colony morphology, gram staining, were followed by a subculture onthechromaticdifferential medium (Liofilchem, Italy) and use of the Analytical Profile Index (API 20E, BioM´erieux, France) provided the presumptive identification of the pathogens[9]. The identity of the Gram-negative bacterial isolates was reported based on the discriminatory power of chromatic medium and API. The presumptive identity of the Gram-positive isolates was reported based on the phe notypic parameters like growth on mannitol salt agar (Oxoid, UK), chromatic agar, colony morphology, and Gram staining and then subsequent microscopical analysis and subjected to an appropriate biochemical test for proper identification. The identity of the Gram-positive isolates was done based on their cultural and biochemical characteristics as reported by Cheesbrough and preserved in 40% glycerol at "80°C[7].

Data analysis was done by descriptive statistics and regression using IBM SPSS version 20. Descriptive statistics was used to obtain UTI prevalence, uro-pathogens frequency, and the mean age. The outcome of UTI was dichotomized as presence or absence of the disease and tested against suspected factors associated with UTI to assess for associations.

The ethical approval of the study was sought from Ethical Review Committee of Anwer Khan Modern Medical College Hospital and research protocols was performed in accordance with the ethical standards of committees on human experimentation laid down in the Helsinki declaration of 1964 revised in 2000[10].

Operational Definition:

Urinary Tract Infection (UTI):

UTI is defined as 10^5 cfu(colony forming unit)/mL of a uropathogen in midstream urine culture from a person experiencing 2 symptoms of cystitis (dysuria, urgency, frequency, suprapubic pain, or hematuria)

or, in the absence of a culture, demonstration of pyuria on urinalysis and 2 urinary symptoms, as well as complete and rapid resolution of symptoms in response to antibiotic therapy for UTI[11,12].

Recurrent UTI:

A recurrent UTI refers to the occurrence of e"2 symptomatic episodes within 6 months or e"3symptomatic episodes within 12 months[2, 12].

Relapse:

A relapse occurs when the same organism is not eradicated from the urine after 2 weeks despite appropriate antimicrobial treatment[12].

Reinfection:

On the otherhand reinfection is usually brought about by a new episode of bacteriuria that is caused by a different strain of bacteria[12].

Results:

In Table I showed a total no of 93 patients were included in the study. Among them 79 were female and 14 were male. Female to male ratio was 5.64:1. Mean age of the patients was 58.61±17.51 (Mean±SD) with age range of 21-85 years. Most of the patients were of 61-70 years age group 23/93 (24.73%) and after that 41-50 years 19/93 (20.43%) (Table I).

Table-I

Distribution of the Patients according to Age(N-93)

Age	No	%
21-30	12	12.90
31-40	9	9.60
41-50	19	20.43
51-60	18	19.35
61-70	23	24.73
71-80	10	10.75
>80	2	2.15
Total	93	100.00

In Table II showed 92.47% (86/93) were married and 7.53% (7/93) were unmarried .

Table-II

Distribution of the Patients according to Marital Status(N-93)

Marital Status	No	%
Married	86	92.47
Unmarried	7	7.53
Total	93	100.00

Table III showed the distribution of patients according to primary disease. Most of the patients were of Diabetes mellitus(DM) 57/93 (61.29%). After that Hypertension, Chronic Kidney Disease(CKD) and CKD + DM about 51/93 (54.84%), 39/93 (41.94%) and 36/93 (38.71%) respectively.

Table-III

Distribution of Patients according to Primary Diseases (N-93)

Primary Diseases	No	%
Diabetes mellitus(DM)	57	61.29
Hypertension	51	54.84
Chronic Kidney Disease(CKD)	39	41.94
DM+CKD	36	38.71
Bening enlargement of prostate(BEP)	7	7.53
Cerebrovascular disease(CVD)	4	4.30
Carcinoma Breast	2	2.15
Impaired glucose tolerance(IGT)	2	2.15
Pregnant	1	1.07

In Table IV showed 54/79 (68.35%) were of menopause and 24/79 (30.38%) women had regular menstrual cycle. 1/79 (1.27%) was pregnant .

Table-IV

Distribution of Patients (Female) according to Menstrual cycle (N-79)

Menstruation Status	No	%
Menopause	54	68.35
Menstrual cycle (Regular)	24	30.38
Pregnant	1	1.27
Total	79	100.00

In Table V showed Escherichia coli(E coli) was the most prevalent uropathogens with 47/93 (50.54%) followed by Klebsiella pneumoniae 12/93 (12.90%), Pseudomonas aeruginosa 10/93 (10.75%), Streptococcus pyogenes 8/93 (8.60%), Staphylococcus aureus 6/43 (6.45%), Enterococcus faecalis 5/93 (5.38%) and others 5/93 (5.38%).

Table-V

Distribution of Patients according to Causative organisms (N-93)

Causative organisms	No	%
Escherichia coli	47	50.54
Klebsiella pneumonia	12	12.90
Pseudomonas aeruginosa	10	10.75
Streptococcus pyogenes	8	8.60
Staphylococcus aureus	6	6.45
Enterococcus feacalis	5	5.38
Others (Proteus mirabilis, Acinetobacter, Corynebacterium, Streptococcus agalactiae, Coagulase negative staphylococcus)	5	5.38
Total	93	100.00

In Table VI showed 77.42% were of relapse and 22.52% were of reinfection.

Table-VI

Distribution of Patients according to Types of Recurrent UTI (N-93)

Types	No	%
Relapse	72	77.42
Reinfection	21	22.58
Total	93	100.00

Table VII showed the Mean±SDof important investigations. The Mean±SD of HbA1c was 7.83±2.15% and that of Serum creatinine and Hemoglobin were 2.17±1.18 mg/dl and 9.82±2.60gm%.

Table-VII

Mean±SD of the related Investigations (N-93)

Investigations	Mean±SD
Serum Creatinine	2.17±1.18 mg/dl
HbA1c (Glycated Haemoglobin)	7.83±2.15%
Haemoglobin %	9.82±2.60gm%

SD- Standard Deviation

In Table VIII On routine examination of urine, 39/93 (41.94%) patient had trace albumin present in urine and 57/93 (61.29%) had reducing sugar. 71/93

(76.34%) had1-2 pus cell in urine and 22/93 (23.66%) presented with plenty of pus cell with 19/93 (20.43%) had 0-4 RBC's (Red blood cell).

Table-VIII

Urine Analysis (N-93)

Urine Analysis	No	%
Albumin (Trace)	39	41.94
Sugar	57	61.29
Pus cell 1-2	71	76.34
Pus cell plenty	22	23.66
RBC 0-4	19	20.43

RBC- Red Blood Cell

In Table IX Factors associated with recurrent UTI were Age >50 years (56.99%), Female gender (84.95%), Married (92.47%), Menopause (58.06%), Diabetes mellitus (61.29%), Indwelling catheter >6 days (25.81%) and Genitourinary abnormalities (15.05%).

Table-IX

Factors associated with Recurrent UTI (N-93)

Factors	No	%
Age>50 years	53	56.99
Married	86	92.47
Female	79	84.95
Menopause (Female)	54	58.06
Diabetes mellitus	57	61.29
Catheters >6 days	24	25.81
Genitourinary abnormalities	14	15.05

Discussion:

In our study the mean age of the patient was 58.61±17.51 years (Range 21-85 years) and majority were female 79/93 (84.94%) compared to male 14/93 (15.06%). However in the study of Odoki M et al the age range of the patients was from 8 months to 95 years and the mean of the study participants was 33.09±23.73 years, which was different from our study[1]. UTI was highest in females with 66/176 (37.50%)as compared to male 20/91 (20.00%) which was near to our study1. The prevalence of bacterial UTI was highest in age group 20-29 with 28/86 (32.60%) in Odoki et al study[1]. In our study it was highest in age group 61-70 with 23/93 (24.73%) as compared to Odoki et al study[1].

E coli was the most prevalent bacterial uropathogenwith 47/93 (50.54%) followed by Klebsiella pneumoniae 12/93 (12.90%) in our study. Similar to our study, in the study of Odoki et al E coli was the most prevalent bacterial uropathogen with 36/86 (41.90%) followed by Staphylococcus aureus 27/86 (31.40%) which is different from our study[1].In our study Staphylococcus aureus was 6/93 (6.45%).

This finding is comparable with other studies elsewhere inAfrica indicating 40–46% of isolation of Ecoli[13-16]. The high prevalence of 27/66(40.9%) of Ecoli in the female gender could be due to the close proximity of the anus to the vagina. This high possibility of UTIs in females is due to the inherent virulence of Ecoli for urinary tract colonization such as its abilities to adhere to the urinary tract and also association with other microorganisms moving from the perineum areas contaminated with fecal microbes to the moist warmth environment of the female genitalia[17,18]. In the study of Odoki et al Staphylococcus aureus was the second most isolated bacterial uropathogen with27/86 (31.40%) of frequency[1]. The high frequency of S. aureus in UTI is not unique to this study. Earlier studies in Bushenyi (Uganda)2015, Mulago (Uganda) 2011,andAwka (Nigeria)2016 reported high rates of S. aureus of 45/103 (43.70%), 9/40 (22.5%), and 60/215 (28%), respectively[19,20,21]. Previous studies have linked the increasing Staphylococcal UTIs to increased use of instrumentation such as bladder catheters[22,23].

Our study demonstrated that age >50 years, female gender, married individuals, menopause, diabetes, genitourinary tract abnormalities, hospitalization, catheter, and increase induration of catheter were found to be a statistically significant relationship with UTIs. Age and female gender were found to have statistically significant relationship with UTIs in similar study carried out by Kabugoet al. in2016 at Mulago hospital in Uganda[24]. The statistically significant association between UTIs and diabetes could be due to altered immunity in diabetic patients which includes depressed polymorphonuclear leukocyte functions, altered leucocyte adherence, chemotaxis, phagocytosis, impaired bactericidal activity of the antioxidant system and neuropathic complications, such as impaired bladder emptying[25,26]. In addition, a higher glucose concentration in the urine may create a culture medium for pathogenic microorganisms in diabetic patients that may result into UTIs. Generally, similar reports from elsewhere also indicated that age, female gender, genitourinary tract abnormalities, diabetes, married individuals, hospitalization, catheter, and duration of catheter be a statistically significant relationship with UTIs[24,27-33].

Conclusion:

This study has demonstrated that hospitalization, married individuals, duration of catheter, diabetes mellitus, genitourinary tract abnormalities, female gender and menopause are the most important factors associated with UTIs. Escherichia coli (E coli) was the most prevalent uropathogens followed by Klebsiella pneumoniae.

Recommendations:

Appropriate measures may help to reduce UTIs due to these associated factors. We recommend routine UTIs screening of patients of the following category: hospitalized, genitourinary tract abnormalities, indwelling catheter, diabetic, female gender, menopause and married individuals. If these routine checks are put in place, prevention of UTI can be realized at lower cost.

Limitations:

Studies focusing on understanding regional differences in UTI epidemiology are necessary, particularly in Bangladesh, where there is currently a paucity of data. The burden of UTIs on both individuals and society is multifactorial and is likely to increase in the context of antibiotic resistance. Both regional and national studies on the burden of UTIs remain an unmet need in Bangladesh.

Data Availability:

The datasets analysed during the current study are not publicly available due to the continuation of analyses but are available from the corresponding author on reasonable request.

Conflict of Interest:

The authors stated that there is no conflict of interest in this study

Funding:

This research did not received any fund

Ethical consideration:

The study was conducted after approval from the ethical review committee of Anwer Khan Modern Medical College & Hospital. The confidentiality and anonymity of the study participants were maintained.

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