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Urinary tract infection in females, a clinicopathological correlation and appraisal

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Abstract

Background: Urinary tract infection is defined as infection of the urinary tract mainly Urethra, bladder and upper tract including Ureter and Kidney leading to significant bacteriuria.

Objectives: The aim of this study was to evaluate and a critical appraisal of the problem of UTI in females with special emphasis on Clinico pathological correlation as prevalent in our society especially problem of recurrent UTI in females under setting of uncomplicated, complicated, recurrent UTI in females.

Material and Methods: This is a retrospective uncontrolled study undertaken in Balrampur Hospital, Lucknow between January to December 2018. Patient population included were females aged 8yrs to 80yrs, who visited OPD and the patients admitted in our hospital indoor during this period, who had nosocomial infection especially with lower Urinary tract symptoms. All the patients were subjected to thorough history taking, clinical, physical examination and urine samples were sent for routine and microscopic examination and for culture where needed. Patients with lower urinary tract symptoms giving history of bladder outlet obstruction or any anatomical or functional disorder of the Urinary Tract were subjected to investigations like ultrasonography, X-Ray KUB, CT and cystoscopy and uroflowmetry studies specially in cases where BOO was suspected.

Results & Conclusions: UTI in females is very prevalent, our study showed on incidence of 18.4% (of all LUTS patients referred for UTI). Nosocomial infections contributed to 38% of UTI cases in our study. Screening for diabetes in UTI patients showed an incidence of 10.3% 30% of HAUTI cases had Indwelling Urinary Urinary Catheter. UTI was most prevalent in 18 to 30 years age group i.e. 41% of all UTI cases in all age groups under considerations. The incidence of RUTI cases was 21%, maximum coming from post menopausal age group. Incidence of ASB was found to be 7%, amongst all 930 patients. In diabetics the incidence of ASB was 11.4%. UPEC was found to be the leading causative agent in both uncomplicated and complicated UTI cases.

Keywords: Urinary Tract Infection (UTI), Recurrent Urinary Tract Infection (RUTI), Hospital Acquired Urinary Tract Infection (HAUTI), Dipstick Test, Lower Urinary Tract Symptoms (LUTS), Asymptomatic Bacteriuria (ASB), CYSTITIS, PYELONEPHRITIS, NOSOCOMIAL INFECTION, UPEC (Uropathogen Escherichia Coli), GBS (Group B Streptococci), K.Pneumoniae (klebsiella Pneumoniae), Mid Stream Urine (MSU) CAUTI (Catheter Acquired UTI).

Introduction

UTIs are inflammatory disorders of urinary tract, where uropathogens get adhered to the urothelium of urinary tract, majority of the uropathogens being *E. Coli*, accounting for almost 50% of infections (Bryan and Reynolds 1984) ^[1]. There are three routes for spreading of infection in females, local colonization of uropathogens in periurethral mucosa of vaginal introitus leading to ascending infection (following sexual activity or urethral instrumentation etc), Haematogenous or lymphatic spread. (Heilberg I.P, Schor 2009) ^[2] postulated ascending infection by uropathogens from vaginal introitus. Nearly 10 to 12% of pregnancies get UTI (Jacociunas *et al.* 2007) ^[3]. UTI can be complicated or uncomplicated. In Uncomplicated UTI one gets frequency, Dysurea, urgency, occasional haematuria, lower abdominal pain but no vaginal discharge but there is no functional or anatomical urinary tract- abnormality (Hooton and Stomm 1997) ^[4]. Complicated UTI is also having LUTS with functional or structural abnormalities (Nicolle 2001) ^[5]. Asymptomatic bacteriuria especially in pregnant ladies should be thoroughly investigated for it may progress into frank upper tract infection, with adverse impact on pregnancy (Nicolle 2005) ^[6]. Recurrent UTI presents as dysuria or irritating voiding symptoms caused by reinfection with original bacterial isolate in young and otherwise healthy women with no anatomic or functional abnormality of the tract. In complicated RUTI there is

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Urinary tract abnormality (Anatomy or function). Frequency of sexual intercourse is strongest predictor of RUTI in young females. In patients with comorbid conditions or other predisposing factors recurrent complicated UTI represents a risk for ascending infection or urosepsis.

E. Coli. is most common microorganism in all patient groups, Klebsiella, pseudomonas, proteus and others are more common with certain risk factors for complicated UTI. In RUTI in post menopausal females there is increased Post Void Residue (On USG) and decreased Urine flow (on Uroflowmetry) whereas in non pregnant premenopausal young females there is no difference in PVR or flow rate (Hooton and Colleagues).

Virulent organisms like Pseudomonas, proteus, MDR *E. Coli.* are the culprits. Host with poor immunity eg. DM, Radiotherapy and chemotherapy recipient, Renal Failure patients, Pregnancy, extremes of age, solitary kidney, transplant patients or reduced capacity of eliminating bacterial infection eg. Foreign body in Urinary tract, obstructive disease (BOO) Neurogenic bladder.

A positive urine culture with greater than 10^3 colony forming units per ml is standard for diagnosing UTI in symptomatic female patients.

Cystitis patients are usually young (Honeymoon cystitis) with positive culture with 10^3 (CFU/ml) Acute pyelonephritis patients have $>10^4$ CFU/ml Asymptomatic bacteriuria 10^5 CFU/ml is to be followed and monitored closely. Microscopic haematuria, Low grade proteinuria and a positive nitrite test along with positive urine culture remain the standard criterion for diagnosis of UTI. UTI patients with LUTS having S/O, BOO/anatomical abnormality may be subjected to USG, CT. X-Ray and Uroflowmetry.

Predisposing factor in healthy young females to get RUTIs are higher PH of vaginal mucosa, short urethra in females, adherence of uropathogen to urothelium, Diabetes mellitus, neurogenic conditions, chronic indwelling catheterisation. These are also important predisposing factors for complicated UTI. The treatment of RUTI infection in female is one of the most difficult challenges for the treating physicians (SCHAPPERT 1994) [7].

Young primiparous women from low socioeconomic status, diabetes and grand multiparity, all predispose to UTI (Wesley *et al.* 2002) [8]. Increased sexual activity, contraception, use of spermicide jelly and diaphragms, and use of antibiotics (eliminates lactobacillus from vaginal flora, which is responsible for maintaining acidic milieu) besides indwelling catheterisation and unhygienic practices like unsanitary absorbent pads all predispose to UTI.

Aim & Objective

A clinico pathological study of UTI in females including uncomplicated, complicated and recurrent UTI especially their peculiar signs and symptoms, risk factors, prevalence of UTI, factors associated with UTI, aetiology, pathology and laboratory profile and assessment of Urinary Pathogens responsible for UTI in both hospitalised and OPD patients.

Review and critical appraisal of Hospital Acquired UTI, community acquired UTI and UTI in different age groups in young, child bearing non-pregnant premenopausal females and older age group post-menopausal females.

Material and Methods

This is a retrospective uncontrolled study undertaken in Balrampur Hospital, Lucknow between January to December 2018. Population comprised of females aged 8yrs to 80 yrs, we picked up patients both from OPD and patients admitted in

Hospital with nosocomial infection suspected of having UTI. Thus patients having Lower Urinary Tract symptoms (LUTS) with UTI were selected for the UTI.

Inclusion Criteria

1. Only Female Patients were selected.
2. Age between 8yrs to 80 yrs.
3. Patients of UTI between January 2018 to December 2018 i.e. One Year Study.
4. OPD patients with LUTS and with most probable diagnosis of UTI.
5. Indoor patients having NOSOCOMIAL (HAUTI) infection.

Exclusion Criteria

1. All male patients.
2. Patients having Overactive bladder (OAB)
3. Vulvovaginitis, Urethritis and Pelvic Inflammatory Disease

OPD patients were subjected to exclusive history taking and physical examination patients giving H/O frequency urgency dysuria, occasional haematuria in absence of vaginal discharge were asked to give Urine for Urinalysis including microscopic examination.

History is taken with a view to exclude Diabetes Mellitus, renal failure, other metabolic diseases, H/O Cancer, patients on chemotherapy, radiotherapy or any other immunodeficiency disease, H/O taking antibiotics, H/o stone disease or any bladder outlet obstruction or neurological disease involving bladder and any other cause of complicated UTI. Uncomplicated UTI patients are usually young, may give H/O frequent sexual intercourse, use of spermicidal jelly or diaphragm, prolonged use of antibiotics. Older women may give H/O incontinence, surgery for incontinence, cystocele etc. For Indoor patients we take history for Nosocomial infections (HAUTI) specially examine patients on indwelling catheter. Elaborate physical examination is done including Pelvic Examination especially costovertebral or renal angle tenderness.

Urinalysis either by dipstick or M/E for detection of Pyuria. A WBC/Leukocyte count of >10 WBC/HPF is pathognomonic of UTI, but its to be done on unspun i.e. uncentrifuged sample of Urine using a haemocytometer chamber Dipstick test for Leukocyte Esterase is done this test is 94 to 98% specific and 75 to 96% sensitive for UTI.

Positive nitrite Test is highly specific (95%) and 35 to 85% sensitive, but its presence is restricted to only 25% of patients.

Microscopic haematuria is supportive of UTI. Low grade Proteinuria is common.

Clean catch Mid-stream Urine Sample (MSU) is collected in sterile, clean wide mouthed, leak-proof bottle after cleaning the urethral area to prevent contamination. In patients with urinary Catheter, urine samples are collected from fresh catheter using a sterile syringe and transferring it to a specimen tube.

Suprapubic aspirate Urine sample may also be taken with a sterile syringe and needle. For culture and sensitivity we use macconkey media (Gram Negative), Blood Agar (Gram positive) and Nutrient Agar for Sensitivity. (Bluish Green pigmented diffusion in medium). Each sample of uncentrifuged, uniformly mixed MSU sample is inoculated on CLED and incubated at 37° aerobically for 24 Hours.

We have based our diagnosis as per given criterion

Urine culture is deemed positive if it shows a bacterial count of greater than or equal to 10^3 colony forming unit per /ml of a typical urinary tract organism.

Results

Pathology department of Balrampur Hospital Lucknow received a total of 13104 Urine samples and this includes both males and females (between January 2018 to December 2018). Both from OPD and indoor patients admitted in wards. Since this study has undertaken review, critical analysis and appraisal of only female patients (between 8 years to 80 years of age) suspected of UTI, we have considered only 5061 female patients, whose samples were collected deleting 8043 male patients out of a total of 13104.

Out of these 5061 patients whose urine was analysed, we could detect UTI in 930 patients as per our criterion. Urine analysis >10WBC/HPF, we found microscopic Haematuria in 409 patients (44%).

Positive Nitrite in 260 patients i.e. 28%. Low Grade Proteinuria in 139 patients i.e. 15%. Hence of all the patients with lower Urinary Tract Symptoms referred, UTI could be detected in 18.4% of patients. (930 out of 5061 patients).

Age wise distribution of these 930 patients was as follows. 8years to 18 years (56 patients i.e. 6%), 18 years to 30 years (381 patients i.e.41%) 30 to 45 years (307 patients i.e. 33%) 45 to 80 years (186 patients i.e. 20%) Hence in our study, maximum UTI cases were patients in age bracket of 18 years to 30 years (41%) followed by patients in age bracket of 30 to 45 year (33%) of all these 930 female patients of UTI.

Out of total of 5061 patients that are under study, 4375 patients were from OPD and 686 patients who were having nosocomial infection were referred from ward (Indoor).

Thus out of a total of 4375 OPD patients 669 were having UTI i.e. 15.3% patients were found to have UTI of all the patients referred from OPD.

Of 686 patients suspected of nosocomial infections from IPD were subjected to Urine Examination and 261 patients i.e. 38% were found to have UTI. The same is tabulated as below:

Table 1: Distribution of patients

OPD	4375	669	15.3%
IPD (ward)	686	261	38%
Total	5061	930	18.4%

Screening for diabetes was done in all these patients of 261 UTI patients from Indoor (ward) 29 patients were found to be diabetic i.e. 11%. Whereas of 669 UTI patients from OPD 67 patients were found to be diabetic i.e. 10%.

If we consider total number of patients from both indoor and outdoor i.e. 930 patients then (29 +67) 96 patients are having diabetes i.e. an over all figure of 10.3% for diabetes patients.

Table 2: Screening for Diabetes in Female UTI patients:

	Total no. of cases		No. of Diabetes
OPD	669	67	10%
IPD (ward)	261	29	11%
Total	930	96	10.3%

Table 3: Incidence of ASB in Diabetic patients is depicted below

Asymptomatic bacteriuria in diabetic patients with UTI	11 out of 96	11.4%
Over all asymptomatic bacteriuria in all UTI patients	65 out of 930	7%

Out of total 261 cases of HAUTI 78 patients were on catheter i.e. 30% The incidence of recurrent UTI (RUTI) cases was 21% (140 out of 669) in OPD patients 55% of all RUTI cases were

from post menopausal age group and 35% of these RUTI cases were from younger age group.

We studied the pattern of bacterial isolates or Uropathogens in both uncomplicated and complicated UTI cases. This study revealed that UPEC was the leading causative Uropathogen (78%) followed by staphylococcus saprophyticus (6%) Klebsiella pneumonia (5%) Enterococcus (4%) GBS (2) Proteus Morabilis 2% Pseudomonas Aeruginosa 1%, Staphylococcus Aureus 1%, Candida 1% in uncomplicated cases. Risk factor associated with these uncomplicated UTI cases were increased frequency of sexual intercourse in young women, use of diaphragm and spermicide jelly, voiding pattern (holding of Urine for long time), faulty wiping pattern prior UTI, diabetes, obesity and genetic susceptibility.

Uropathogens amongst complicated UTI patients were found to be maximum UPEC (60%) followed by Enterococcus spp (13%), Klebsiella (7%), Staphylococcus Aureus 4% candida (6%), staphylococcus saprophyticus 2%, GBS 2%, proteus mirabilis 3%, pseudomonas aeruginosa 3%. Risk factors were diminished host resistance as in Diabetes, immunocompromised patients, patients on RT and CT for malignancy, pregnancy, indwelling catheter related risk factors, urinary tract abnormality of anatomy and function, stones, strictures or cystocoele, postmenousal women, neurogenic bladder. Of all the 96 Diabetic patients, only 11 patients i.e. 11.4% were found to be having asymptomatic bacteriuria. Overall ASB was found in 65 out of 930 UTI patients i.e. 7%. ASB patients are those having 10^5 CFU/ml but not having any symptoms.

Discussion

Urinary tract infections (UTIs) are the inflammatory disorders of the urinary tract caused by the abnormal growth of pathogens. Urinary tract infection is known to cause short-term morbidity in terms of fever, dysuria, and lower abdominal pain (LAP) and may result in permanent scarring of the kidney. Urinary tract infections can be community acquired or nosocomial. Community-acquired urinary tract infections (CA-UTIs) are defined as the infection of the urinary system that takes place in one's life in the community setting or in the hospital environment with less than 48 hours of admission. Community-acquired UTI is the second most commonly encountered microbial infection in the community setting. Nosocomial urinary tract infections (N-UTIs) are the infection of the urinary tract that occurs after 48 hours of hospital admission, and the patient was not incubating at the time of admission or within 3 days after discharge.

In this study we included a total of 5061 (4375 from OPD and 686 from IPD) patients. Out of all these patients UTI could be detected in only 930 patients i.e. 18.4 % of patients.

If we analyse this data of confirmed UTI cases it was found that UTI was found to be most prevalent in 18 years to 30 years age group (381 out of 930 i.e. 41%) and least prevalent is 8 to 18 years age group (56 out of 930 i.e. 6%) Figures for OPD and IPD patients stood at 15.3% and 38% respectively. Thus of all the Nosacornial infections referred for Urine examination HAUTI was found in 38%.

Screening for Diabetes in confirmed UTI cases revealed that 29 patients out of 261 UTI patients from ward (IPD) i.e. 11% were diabetic and 67 patients out of a total of 669 UTI patients from OPD i.e. 10% were diabetic. Thus we found an overall incidence of 10.3% of Diabetic patients (96 confirmed patients of Diabetic out of 930 patients).

78 patients out of these 261 cases of HAUTI were on indwelling catheter i.e. 30% of nosocomial UTI cases Uropathogens

involved in causation of UTI in these catheter induced UTI (CAUTI) were *E Coli*, proteus, pseudomonas, candida and Enterococcus.

Our study revealed incidence of ASB to be 11.4% (11 out of 96 Diabetes patients) and over all incidence of ASB considering all our UTI case was 7% (65 out of 930 patients). We observed that rate of ASB in Urine increases with age, least in child bearing age group and maximum in elderly post menopausal women.

We found uropathogens klebsiella, Gr. B streptococci and enterococci besides *E Coli*. in Diabetic pts with UTI.

Conclusion

Prevalence of UTI in females is much higher as compared to males, in our study we found that patients with symptoms of LUTS suspected to be having UTI, 9.5% of males had UTI as compared to 18.4% for females. For OPD patients the figure of UTI patients was 15.3% whereas for IPD patients with nosocomial infections. UTI was found in 38%. Thus figure of HAUTI is much higher than OPD patients. 11% of Indoor patients with UTI had Diabetes as compared to only 10% Diabetics of all the UTI patients from OPD. Thus overall figure of Diabetes was 10.3% of all female UTI patients. 30% of HAUTI patients had indwelling Urinary Catheter. Maximum number of UTI cases were from 18yrs to 30yrs age group amounting to 41% of all UTI cases. The incidence of recurrent UTI cases was 21%, majority of RUTI cases were from Post-Menopausal Age Group accounting for 55% of total RUTI cases.

Out of a total of 669 UTI cases from OPD 140 cases could be levelled as RUTI cases i.e. recurrent UTI (3 episodes of UTI in a year or 2 episodes in 6 months) and 21% of OPD patients were that of recurrent UTI Out of 140 cases of RUTI, 77 were in aged (45-80) i.e. post-menopausal or 55% of all RUTI cases were post-menopausal. 49 patients were from younger age group i.e. 35%.

Incidence of ASB was 7% in our study of total of 930 UTI cases. If we consider only Diabetes patients with UTI, this figure for ASB was 11.4%. We observed that rate of ASB in Urine increases with Age being maximum for elderly post-menopausal women and least for young child bearing age group females.

UPEC was found to be the leading cause of uncomplicated UTI amounting to 78% of all causative Uropathogens. Risk factors being increased frequency of sexual intercourse, use of spermicides jelly, diaphragm, faulty voiding pattern, faulty wiping technique, Diabetes and obesity besides genetic predisposition. Of all the Uropathogens associated with complicated UTI.

UPEC had the maximum share of 60% followed by Enterococcus spp (13%). Risk factors were Immunosuppression, Indwelling Urinary Catheter, abnormality of structure or function of Urinary tract, Neurogenic Bladder.

Thus there is a need for educating the masses specially the young female about healthy sexual practices use of uncontaminated and clean sanitary pads, importance of taking lot of water and frequent voiding, use of correct wiping technique. Correction of Anatomical or functional Urinary tract abnormality, treatment of stones, strictures and cystocoele correction, specially in post-menopausal women and use of oestrogen jelly if indicated in older women. Will all go a long way in preventing and containing UTI. Patients having recurrent UTI and females having ASB need to be watched carefully and treated promptly whenever the need arises.

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