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EVALUATION OF PYURIA IN BUNDELKHAND REGION

Nephrology

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ABSTRACT

Introduction: This study was undertaken to find out the **Prevalence of Pyuria in Bundelkhand region** and to assess the validity of microscopic urine analysis and dip stick test in the diagnosis of pyuria.Pyuria is defined as the presence of 10 or more white cells percubic millimeter in a urine specimen, 3 or more white cells per high-powerfield of unspun urine, a positive result on Gram's staining of an unspun urine specimen, or a urinary dipstick test that is positive for leukocyte esterase.

Aims and objectives: To determine the prevalence of pyuria in all patients in Bundelkhand region, To determine the validity of urine RM in febrile patient in Bundelkhand region, Study the accuracy and clinical application of dipstick leukocyte esterase test in the detection of pyuria and To study all cases of pyuria

Material and methods: A cross sectional study was undertaken in the department of Medicine,in collaboration of department of Pathology and department of Microbiology, M.L.B. Medical College, Jhansi. Urine was collected from enrolled patients and sent for routine microscopic examination as well as for culture and sensitivity. **Results:** 100 patients were enrolled in this study out of which 71 case showed presence of pus cells in urine,out of which 64 cases were positive for urine culture and senstivity.Chi-square analysis was done for significant pyuria (>5 pus cells/ HPF) and a sensitivity of 100% was calculated with accuracy rate of 97.5%.

Conclusion: Pyuria is more common in middle aged sexually active females and old age males with urinary tract obstructive pathology**.** Pyuria is more common in cases with long standing urinary catheterisation. Pyuria is more common in patients with other comorbidities like DM, CKD. Urine culture is the gold standard for diagnosing pyuria. Microscopic urine analysis is a strong tool and is helpful in diagnosing UTI. To reduce pyuria in In patients catheterisation should be done in aseptic condition with proper precaution to prevent UTI. Deep stick test is not reliable for diagnosis of pyuria.

KEYWORDS

Urinary Tract Infection, Microscopic Urine Analysis

INTRODUCTION

Pyuria is defined as the presence of 10 or more white cells per cubic milli meter in a urine specimen, 3 or more white cells per high-power field of unspun urine, a positive result on Gram's staining of an unspun urine specimen, or a urinary dipstick test that is positive for leukocyte esterase[1].

It is a relatively common problem, with a wide range of causes, encountered frequently in both primary and secondary care settings, although there is no data to suggest the estimated prevalence in either a community or hospital setting. Indeed, the medical literature, in all its vastness, contains remarkably little research or guidance regarding this problem, leaving many primary care physicians in the dark as to how best to manage their patients. This results in inconsistent management, ranging from ignoring the finding completely to over investigation and possibly unnecessary secondary care referral.

It is an evidence of acute inflammation. However, pyuria is not always associated with bacteriuria and its absence does not exclude infection. Leucocytes are normally absent in midstream urine from healthy children and male subjects. The urine of adult women frequently contains leucocytes and a small number should be regarded as normal. Ten cells per cubic mm in uncentrifuged urine is the upper limit of normal leucocyte excretion. The presence of 100 pus cells per cubic mm in uncentrifuged urine specimens correlates well with infection.

Varying urine white blood cell (WBC) thresholds have been recommended for abstract the presumptive diagnosis of urinary tract infection (UTI) among young infants. These thresholds have not been studied with newer automated urinalysis systems that analyze uncentrifuged urine that might be influenced by urine concentration. Evaluation to detect bacterial, fungal, and parasitic infections is indicated in patients with a clinical history that suggests specific infections[2].

Abdominal, renal, and bladder imaging should be considered for evaluation of febrile or otherwise symptomatic patients. Inflammatory conditions near the urinary tract as well as systemic diseases should be included in the differential diagnosis. Sterile pyuria has historically been considered to be suggestive of genitourinary tuberculosis, but a wide variety of other causes must be considered.

There are many overlaps between the finding of pyuria and that of asymptomatic non-visible haematuria – both are fairly common incidental findings, both with relatively low risk of significant underlying pathology, but both with potential causes that we would not want to miss. The recommended management of non-visible haematuria in primary care is now well described, but guidance on pyuria is entirely absent. This article aims to provide a framework for assessing patients with pyuria, but in the absence of a good evidence base must represent basic guidance only, with individualised management decisions required when faced with this problem in primary care.

If pyuria is seen on microscopy in the absence of prior dipstick analysis, it is unclear on the exact threshold for clinical significance, although a value of >10 white blood cells per µl of urine may be sensible.

It is important to ensure that a urine specimen is taken clean-catch and mid-stream to reduce the risk of contamination. Urine from catheters or urostomies will almost always contain white cells and cannot therefore be interpreted, except in the context of symptoms, e.g. of suspected infection.

Again, to be consistent with non-visible haematuria guidelines, it would appear sensible to consider a dipstick showing only a trace of leucocytes to be a negative result, which can be safely ignored, and to treat "+" or greater as a positive result. There is no prognostic difference between "+" or "+++" of red blood cells for patients with non-visible haematuria – it is not known whether the same applies in sterile pyuria, but it would seem to be a reasonable assumption. An MSU is sent to allow urine culture to detect the presence of organisms, and not to confirm the presence of leucocytes, which may degrade while in transit to the laboratory, thus creating a false negative result[3].

Urinary tract infection cannot be diagnosed on clinical grounds alone. Confirmation of UTI requires documentation of bacteria in bladder urine. However, the culture in clinical practice is usually done on voided urine which in women is easily contaminated with perineal bacteria. Quantitative culture and specific identification of the organisms in urine are used to distinguish contamination from true urinary tract infection. Bacterial counts by conventional methods are difficult to adopt in an ordinary diagnostic laboratory and are expensive intime and material. The simple methods like calibrated loops, blotting papers, strips and dipslides also require overnight incubation. As an alternative to the conventional methods, several presumptive tests are available which either quantitate bacteria by non-cultural methods or suggest infection by the demonstration of an inflammatory reaction. Such tests are microscopy for pyuria and bacteriuria, chemical tests for detection of pus cells and bacteria in urine and automated methods for bacteriuria detection.

Complicated urinary tract infections (UTIs) occur in the setting of a urinary tract that has metabolic, functional, or structural abnormalities. Complicated UTIs may involve both lower and upper tracts .Their primary significance is that they significantly increase the rate of therapy failures.

The pathophysiology of complicated UTIs has the following 4 aspects:

- Structural abnormalities, such as calculi, infected cysts, renal/bladder abscesses, certain forms of pyelonephritis, spinal cord injury (SCI), and catheters
- Metabolic/hormonal abnormalities, such as diabetes and pregnancy
- Impaired host responses, such as transplant recipients (especially renal transplants) and patients with AIDS
- Unusual pathogens, such as yeast

A growing number of complicated UTIs are healthcare associated in origin. The most common pathogens include *Escherichia coli,* enterococci, *Pseudomonas aeruginosa,* candidal species, and *Klebsiella pneumoniae.*

Pyelonephritis is almost always the result of bacteria migrating from the bladder to the renal parenchyma, which is enhanced by vesicourethral reflux. In uncomplicated pyelonephritis, the bacterial invasion and renal damage are limited to the pyelocalyceal-medullary region; in complicated pyelonephritis, all regions of the kidney may be affected. If the infection progresses, bacteria may invade the bloodstream, resulting in bacteremia[4-5].

Microscopy of urine for bacteriuria is a rapid screening technique which has been used for years as a standard laboratory practice[6]. Urine can be examined stained or unstained and centrifuged or uncentrifuged. The most widely used method is the Gram stained smear of fresh uncentrifuged specimen of unne examined under oil immersion objective. Visualizing any bacteria by this technique is reported positive, with the sensitivity being 69 to 96%[7-10].

As Enterobacteriaceae, the most prevalent orpnisms found in infected urine, reduce nitrate to nitrite[11-12]. So the nitrate reduction test is a useful tool and nitrite detection is an indicator of UTI[13]. Presence of blood or protein in the urine detected by multipatch strips also indicates urinary tract infection[14-15]. Sensitivity of more than 85% and negative predictive value of more than 86% has been reported[16]. Pyuria can also be assessed with distrips. The estcrases present in neutrophils are detected with the help of a dipstrip. This parameter with the presence of blood, protein and nitrite in urine gives a sensitivity from 91% to 94% and negative predictive value from 89% to 95%.

The present study compares the screening of urine by Gram staining and evaluation of pyuria assessment in uncentrifuged urine with the dipstick tests for blood protein present and leucocyte esterase.

AIMS AND OBJECTIVES

- To determine the prevalence of pyuria in all patients in Bundelkhand region.
- To determine the validity of urine RM in febrile patient in Bundelkhand region.
- Study the accuracy and clinical application of dipstick leukocyte esterase test in the detection of pyuria.
- To study all cases of pyuria

MATERIAL AND METHODS

Our study was a prospective observational study & was conducted in M.L.B. Medical College, Jhansi. During the period from May 2019 to Oct. 2020, 100 patients were included in our study. Hundred specimens of urine were obtained from both patients and in-patients of Pyuria in Medicine Department and collaboration with Department of Pathology ,Department of Microbiology, M.L.B Medical College, Jhansi (U.P.).

ETHICAL CONSIDERATIONS

Informed written consent were obtained from the patients attendants and the study was approved by the Hospital's Ethics Committee.

INCLUSION CRITERIA

- All febrile patient > 18 yrs.
- Acute (i.e. symptoms less than 28 days) and UTI as a main diagnosis.
- AND 1 clinical symptoms (core body temperature 38^0C, urgency, frequency of micturition, dysuria, suprapubic pain, flank, costovertebral angle tenderness, nausea and vomiting)
- AND 1 urinary criterion (pyuria (> 20 leukocytes/l) and/or nitrites in patients without antibiotic pretreatment.
- Informed consent by patient or available relative or an independent physician.

EXCLUSION CRITERIA :

- Patient < 18 yrs and > 80 yrs.
- Any patient who has received antibiotics 48 hours prior to evaluation will not be included in the study.
- Patients with known congenital genitourinary anomalies.
- Brief history of patients will be obtained and patients on antibiotics will be excluded.
- Attendant not willing to enroll the patient.

METHODS:

- **Febrile Patients:** Patients with history of fever (Temperature; rectal ≥38.3°C or axillary temperature ≥37.8°C).
- **Urinary Tract Infection:** Urinary tract infection is defined as growth of a significant number of organisms of a single species in the urine, in the presence of symptoms. Significant bacteriuria is growth with a colony count of $>10^5$/ml of a single species in a mid - stream clean catch urine sample.

Febrile patient > 18 yrs and < 80 yrs attending OPD / IPD or admitted in MLB Medical College & Hospital Jhansi will be submitted to preliminary screening interview to suspect urinary tract infection. Patients with symptoms suggestive of urinary tract infections will be enrolled and interviewed using structured questionnaire for urinary tract infection. All symptomatic children will be referred for urine routine microscopy and culture tests.

Collection of urine sample:

From all 100 cases a sample of urine was collected. In patients with folye's tube urine was collected by a bag and in others midstream sample was collected.

Investigations and treatment

First, urinalysis is the prime investigation for SP. Importantly, SP is not always sterile, so repeating cultures often yields a positive result on subsequent testing. Contamination, especially with vaginal leukocytes in females, is common, and samples should always be collected as a midstream clean catch. The use of antiseptic solutions prior to collection should be avoided to limit false-negative tests.

Urine samples from each patient were labelled and immediately transported to the laboratory where they were gently shaken and divided into two aliquotes. In case of delay, samples were kept at 4°C and analysed within two hours of collection.

Practice nurses may also encounter a previously undiagnosed SP during routine screening tests, or disease monitoring in patients with long-term conditions like diabetes. At this juncture, sending urine for culture and sensitivity is recommended, with onward advice to see their GP for further investigation, pending results.

Second, routine haematological tests including a full blood count, renal, and liver function tests are of paramount importance. Swabs for *Chlamydia* and *Gonorrhoea* are recommended for sexually active

patients. If urinary tuberculosis is suspected, three consecutive first-void morning samples are required for acid-fast bacilli and polymerase chain reaction (PCR) testing.[2]

Eosinophilia is an important marker of drug-induced interstitial nephritis, but may also be seen in schistosomiasis. In suspected schistosomiasis, a terminal urine sample should be collected between noon and 3 pm, to coincide with maximal egg excretion.

Third, the choice of imaging modality depends on the history and findings on examination. A renal tract ultrasound scan or computerised tomography is recommended when renal stones, masses, or nephritis are differential diagnoses. Endourological procedures such as rigid or flexible cystourethroscopy and tissue sampling are undertaken if tumours are suspected, but they also have the advantage of diagnosing and treating benign pathologies such as bladder stones

Microscopic examination:
Using the Fuchs-Rosenthal cell counting chamber, uncentrifuged urine from the same urine sample will be examined under the light microscope by the doctor on call, who will be not aware of the dipstick LE test result. A leukocyte count of ≥10 mm3 (≥0.01 x 109 /L) will be taken to be a positive result.

Statistical methods:
SPSS (Statistical Package for Social Sciences) version 14.0 and Graph Pad (online) for windows will be used for data analysis. Mean and standard deviation are descriptive values for quantitative data with median and range for non-normally distributed data. Student's t-test and non-parametric t-test (Mann Whitney test) will be using comparing means of two independent groups. Paired t-test and non-parametric paired t-test (Wilcoxon signed rank test) were used for comparing means of two dependent groups. Chi-square – Fisher exact test were the tests for proportion independence. Receiver operating characteristic (ROC) curve will be used to define the cutoff value and its sensitivity and specificity for prediction of LV dysfunction at the end of follow-up period. p-value < 0.05 is considered significant. Graphics were designed by Microsoft Office Excel 2007/10.

Urine analysis with urine routine microscopy and urine culture is required to diagnose Urinary tract infection.

RESULT

Table 1: Pyuria is defined as the presence of 10 or more white cells per cubic milli meter in a urine specimen

Pus cells	Number of cases	Percent
Present	71	71.00%
Absent	29	29.00%

Table 2- Gender wise distribution pyuria n=71

Sex	Number of patients	Percent
Female	42	59.15%
Male	29	40.85%
F:M	42:29	

Table 3- Sexual profile pyuria distribution n=71

Sexual profile	Number of patients	Percent
Active	39	54.93%
Inactive	32	45.07%

Table 4: Age/sex/sexual profile n=71

Age in years	Female		Male	
	Active	Inactive	Active	Inactive
18-30 years	3	0	1	0
31-60 years	16	5	10	0
61-80 years	1	17	8	10

Table 5: Dipstick leukocyte esterase test results(n=100)

Test Result	Number of patients
Positive	40
Negative	60

Table 6: Risk factors(n=71)

Risk factors	Number of cases	Percentage
Present	52	73.24%
Absent	19	26.76%

Table 7: Urine culture sensitivity results (total patients=71)

Pathogen	Number of patients	Percentage
Candida species	6	8.45%
E.coli	60	84.51%
Kleibsiella	13	18.31%
Enterococcus species	2	2.82%
Proteus	5	7.04%
pseudomonas	3	4.23%
Staph saprophyticus	1	1.41%
Sterile	7	9.86%

DISCUSSION

This study was a hospital based cross-sectional study entitled 'EVALUATION OF PYURIA IN BUNDELKHAND REGION' conducted in MLB Medical college, Jhansi (UP).The study included patients from both OPD and IPD study was conducted after obtaining permission from the institutional ethics committee and the identity of the patients would not be revealed.

Out of 100 patients, total 71 pts were positive for pyuria .Out of 71 patients with pyuria 51 patients in our study were males and 29 were females showing female preponderance. The mean age of the patient in this study was 58.59±15.17 years, ranging between 18-80 years. The mean age of our patients is older than that of Annei *et al*[14] who reported mean age of 48 years and Richard glazier *et al*[15] who reported mean age of 47 years. However, Eugene *et al*[16] reported higher mean age of 60 years .

Logistic regression was done to find the association between probable pyuria and different risk factors like age, gender, education and duration of disease. Among those who had probable pyuria nearly 59.9% were women. The women having pyuria is 5.15 times (95%CI 1.69-15.89, (p 0.004) higher than the odds of men having pyuria. Only 29 men were diagnosed to have probable pyuria out of which 8 belonged to the age group 57 years and above. Older age group has 5 times more risk of having pyuria compared to younger age group. (p0.002)

No statistically significant association was noticed between probable pyuria and educational status and duration of disease.

A hospital based cross sectional study was carried using urine dipstic which would measure both nitrite level and leukocyte esterase level in urine. Enterobacteriaceae which is one of the common causes of UTI produce nitrite from nitrate which can be detected using dipstick. Similarly, the leukocyte esterase test identifies the esterase produced by the neutrophils, both intact and lysed. Positive nitrite and leukocyte esterase test is indication of pyuria. It is not a confirmatory though. The gold standard for confirming pyuria is urine culture test. Studies have shown the sensitivity and specificity of leukocyte esterase and / or nitrite test is 67 to 100% and 67% to 98% respectively. True prevalence can be calculated using the formula (apparent prevalence + specificity - 1)/(sensitivity+ specificity-1). The apparent prevalence of pyuria using urine dip stick is 26.5%. Thus the true prevalence will be between 19.1% and 25%.

Pyuria was found to be more among women and older age group. Men are less prone to pyuria but the prevalence increases with age and this could be because of obstructive uropathy and voiding dysfunction associated with prostatic hypertrophy.

In our study Pyuria was significantly associated with the occurrence of fever and chills ($p < 0.0001$), with gram-negative bacterial species being relatively more pyogenic than gram-positive species.

Semiquantitative urine cultures were performed by using standard techniques. A positive urine culture was defined as growth of a single uropathogen at a concentration of ≥50 000 colony-forming units per milliliter from a catheterized specimen or a single uropathogen at a concentration of ≥100 000 colony forming units per milliliter from a clean-voided specimen.

To determine the degree of pyuria, urine WBCs were counted either per high-powered microscopic field (hpf) or per cubic millimeter. The former was performed by using the IRIS urine chemistry analyzer (Iris Diagnostics, Chatsworth, CA), whereas the latter was performed manually by a laboratory technician using a hemocytometer. The type

of test performed depended on the ordering physician's preference. No child had both tests performed. Pyuria was defined by the presence of a significant number of WBCs on microscopic urinalysis (≥5/hpf or ≥10/mm3). A positive leukocyte esterase (LE) test on the urine dipstick was defined as 1+, 2+, or 3+ LE (0 or trace were considered negative).

CONCLUSIONS

- The most frequently isolated organisms were E coli, Klebsiella species (41 K pneumoniae, 5 K oxytoca), Enterococcus species (34 E faecalis, 1 other), Proteus species (29 P mirabilis, 2 other), and Enterobacter species (13 E cloacae, 2 other) representing 85%, 4%, 3%, 3%, and 1% of positive urine cultures, respectively. C. Prevalence of pyuria was higher in elderly patients. (50.7%) i.e prevalence of pyuria increase with age.
- Prevalence of pyuria was higher in female (59.9 %)
- Middle age females who were sexually active had higher incidence of pyuria (16.2%).
- Prevalence of Catheter associated pyuria was 47.2 % in female patients.
- Incidence of Hospital acquired/nosocomial infection were 80%.
- Prevalence of pyuria was higher in patients with risk factors (73%).
- Prevalence of pyuria was higher in elderly males with BPH.
- In non catheterised patients ,prevalence of pyuria was higher in patients with DM.(48%)
- Prevalence of association of E.Coli with pyuria was 84.1%
- 77.6% patients with pyuria presented with symptoms like ,dysuria, supra pubic pain, frequency, flank pain etc
- 7.22 % pts had asymptomatic pyuria.
- 42 % patients of pyuria presented with fever
- Sensitivity Urine routine and microscopy came to be about 94%.
- 5.6% pyuria cases were sterile.
- Dip stick test is not reliable in predicting UTI and we suggest performing urine culture and sensitivity for patients in admitted with suspected UTI.

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