International Journal Dental and Medical Sciences Research
Volume 2, Issue 3, pp: 54-62 www.ijdmsrjournal.com ISSN: 2582-6018

The usefulness of urine cytology in 290 routine voided sampleswith hematuria and follow up with histopathology in 60 cases.

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Date of Submission: 30-08-2020 Date of Acceptance: 15-09-2020

ABSTRACT; Aim of the study – To determine the utility of urine cytology in patients presenting with hematuria and re-evaluated the microscopic features in all cases and to diagnose presence or absence of atypia using Paris system of reporting Urine cytology and followed up with histopathology.
Materials and methods – In this study out of 290 patients presenting with hematuria to the tertiary care hospital during the period of one year (November 2017-october 2018).only 60 patients had histopathology correlation. In addition all the patients have evaluated for upper and lower urinary tract by cystoscopy to R/O any pathology.
Results - These 290 cases were classified into two broad categories as: negative and positive for atypia. Majority of cases i.e. 229(78.9%) cases were negative for atypical cells whereas 61(21.1%) cases showed presence of atypical cells. 61 cases with atypical cells were evaluated using Paris system of reporting urine cytology.
Conclusion –Urine cytology followed by histopathology is the gold standard in the diagnosis of patients with hematuria.
KEY WORDS –Hematuria, Paris system, urine cytology, Histopathology, Atypia, malignancy

I. INTRODUCTION

Gross or microscopic hematuria ≥3 red blood cells (RBC)per high power field[(1)]may be caused by numerous factors - urinary calculi, hematologic abnormalities, infection,trauma, tuberculosis, and tumor[(2)]Some of thesefactors (e.g., tumor) may be life threatening. Thus prompt,thorough evaluation and treatment are needed.

Urine for cytology can detect cancerous cells shed fromany part of the entire urothelium (i.e., collecting system tourethra) in a voided urine specimen. Higher grade tumorsor larger tumors (> 3 cm) are more likely to shed cells intothe urine and thus the sample is more likely to be positivefor cancer. Urinary cytology has a notoriously low sensitivity,but an extremely high specificity, thus making it auseful tool in following patients with high grade cancers[(3,4)]. Furthermore, interpretation of urinary cytology maybe difficult, especially in the face of such conditions as urinarytract infection. Here, we report the utility ofurinary cytology of patients presenting to a urology clinicfor evaluation of hematuria and re-evaluating the cases positive for atypical cells using Paris system of reporting urine cytology. Currently,evaluation for the hematuric patient consists of inspecting the lower urinary tract by cystourethroscopy andthe upper urinary tract with computed tomography scan (CT) of the abdomen and pelvis with and without intravenous contrast, ultrasonography or intravenous pyelogram (IVP), and obtaining a urine sample for cytologic evaluation[(5,6)].

II. MATERIALS AND METHODS

Case selection – Fromthe lab information system we retrieved all the urine samples ofhemturia patients from September 2017 to September 2018.
The following parameters were taken into consideration, date of collection, clinical history and type of urine sample.
Smear preparation –The voided urine specimens were prepared by conventional methods like cytospin and centrifugation. All the slides were stained with Hematoxylin and Eosin and special stains(PAS,GMS) were done whenever necessary.
The Paris system of cytological classification included the following categories
A) Negative for atypical cells – Benign
Reactive
B) Atypical Urothelial cells
C) Suspicious of urothelial carcinoma
D) Urothelial carcinoma – High Grade carcinoma/Low grade neoplasia
E) other malignancies, metastasis/miscellaneous lesions
These cases were confirmed with histopathology where ever possible.

III. RESULTS

Of the 290 patients presenting for evaluation of hematuria, an average ageof 60 yrs (34 to 87 years) with 201(69.2%) male and 89(30.7%) Females . These cases were further evaluated and the samples were further processed for cytology, **Table 1** depicts the demographicand clinical characteristics of all 290 patients presenting for evaluation of hematuria.
Specimen type –the samples collected were routine voided samples in all 290 cases.
Clinical presentation –the patients were evaluated for hematuria, 91 patients had no other findings, 72 – urinary tract infection,06-renal cysts,16-stones(ureter,kidney,bladder),10 – benign prostatic hyperplasia ,21 – mass lesion detected in bladder,37-miscellaneous symptoms,37 cases no history and examination details are provided.
Cytological diagnosis- Based on presence or absence of atypical cells on cytology, these cases were classified into two broad categories as: negative and atypia[7].Cases with atypia are re-evaluated and classified using paris system. Majority of cases i.e. 229(78.9%) cases were negative for atypical cells where 61(21.1%) cases showed presence of atypical cells. These 61 cases were correlated with histopathology. Table -2 and Table -3 depicts the reports of cases from negative and positive for atypical cells in urine cytology.

IV.DISCUSSION

The primary goal of Paris system working group was standardizing the terminology for reporting urine cytology based upon histopathology and clinical outcome. Our study indicates that the prevalence of bladder cancer in patients presenting with hematuria is high (71%). None of patients in the study had apositive cytology and a negative cystoscopy /radiologicevaluation.

Hematuria is the most common presentation in bladdercancer patients and some patients have asymptomatic microscopic hematuria but positive for urine cytology[8].Thus the diagnosis of bladder cancer is combination of radiology, cystoscopy, biopsy and urine cytology. Radiology and urine cytology is a non-invasive technique suitable for screening, diagnosis and follow-up[9]. Urine cytology can detect carcinoma in-situ, low grade tumor, and most of the aggressive neoplasm. Urinecytology can detect bladder malignancy more accurately if the grade of the tumoris high[10,11]

A variety of lesions can lead to exfoliation of transitional cells including inflammatory process, infection, stones, and trauma (surgical, instrumentation). Chances of false positive diagnosis can occur in urinary cytology compared to other techniques. In addition, due to marked variation in size and shape of transitional cells, exhibit nuclear and cytoplasmic degenerative changes that can mimic malignancy [15]

Also, it has been shown that patients with negative cytological findings have a very low risk of recurrence, while high-grade cytological abnormalities predict an aggressive tumor course.[12] Apart from these, urine cytology is also a better indicator of the

presence of urothelial atypia, and indication for mucosal biopsies[13]

In our study, we found that about 21.1%(61 out of 290 cases) of hematuria patients were positive for malignant cells in urine cytology. 51 cases had biopsy for histopathology.But still it is not possible to localize cancer based on urine cytology alone. A positive test warrants further evaluation and investigation of the patient [14]

Out of 24 cases of malignancy in cytology, 21 cases diagnosed as urothelial carcinoma. Of these 21 cases, 01 case diagnosed as squamous cell carcinoma (Fig1A,1B,1C)06 cases are low grade and remaining are high grade urothelial carcinomas in histopathology (Fig 2A, 2B, 2C, 2D).The cases in the suspicious category are both low grade and high grade urothelial carcinomas in equal proportions in histopathology i,e 03 cases each.

In our study, 19 cases had atypical cells in the background of inflammation. In the atypical category 02 cases were diagnosed as low grade urothelial neoplasms (Fig 3A, 3B), 11 cases turned out as nonspecific cystitis (Fig 4A, 4B) and 02 cases as eosinophilic cystitis in histopathology.These are the cases of less consequence and correlated clinically and confirmed by histopathology. Thus,interpretation of urine cytology should always be used as an adjunct to clinical data along with other diagnostic tools[16]

Of these 229 negative cases in the study, 133(58.1%) cases showed signs of acute or chronic inflammation with presence of some degenerated cells, 76(33.1%) cases showed nonspecific pathologyand remaining 20(8.7%) cases were non-contributory without any clinical, radiological and cystoscopic data. But only 19/229 cases had follow up.

In these 19 cases, 01 case each as papilloma (Fig 5A,5B), papillary urothelial hyperplasia(Fig 6A, 6B)and urothelial carcinoma insitu, 02 cases turned out as low-grade non-invasive urothelial carcinomas, 05 cases as tuberculous cystitis (Fig 7A,7B)09 cases as nonspecific cystitis (Fig 8A,8B).

A negative cytology doesn't always exclude malignancy. There are several reasons for these diagnostic inaccuracies, as urine is an inhospitable environment for cells; consequently cells undergo degenerative changes which can make diagnosis difficult [17]

According to American urological association (AUA) recommendations, urine cytology is reserved only for patients with risk for TCC[18] it is considered as a good tool for screening in middle-aged or elderly patients.[19] Due to its subjectivity and lack of uniformity in reporting, urinary cytology is used as a screening technique in correlation with other imaging and clinical findings.

V. CONCLUSION

Patients with suspicious urinary cytology with negativeinitial evaluation should have repeated urinary cytologyanalysis carried out at least six to eight weeks later.

Asymptomatic patients or patients with obvious benignpathology do not require repeat evaluation.

Those with persistent positive cytology or recurrenthematuria need further evaluation and follow up andcareful evaluation of the prostate should also be carried outin these patients.

Acknowledgements–
None
Funding –
None
Competing interests –
None

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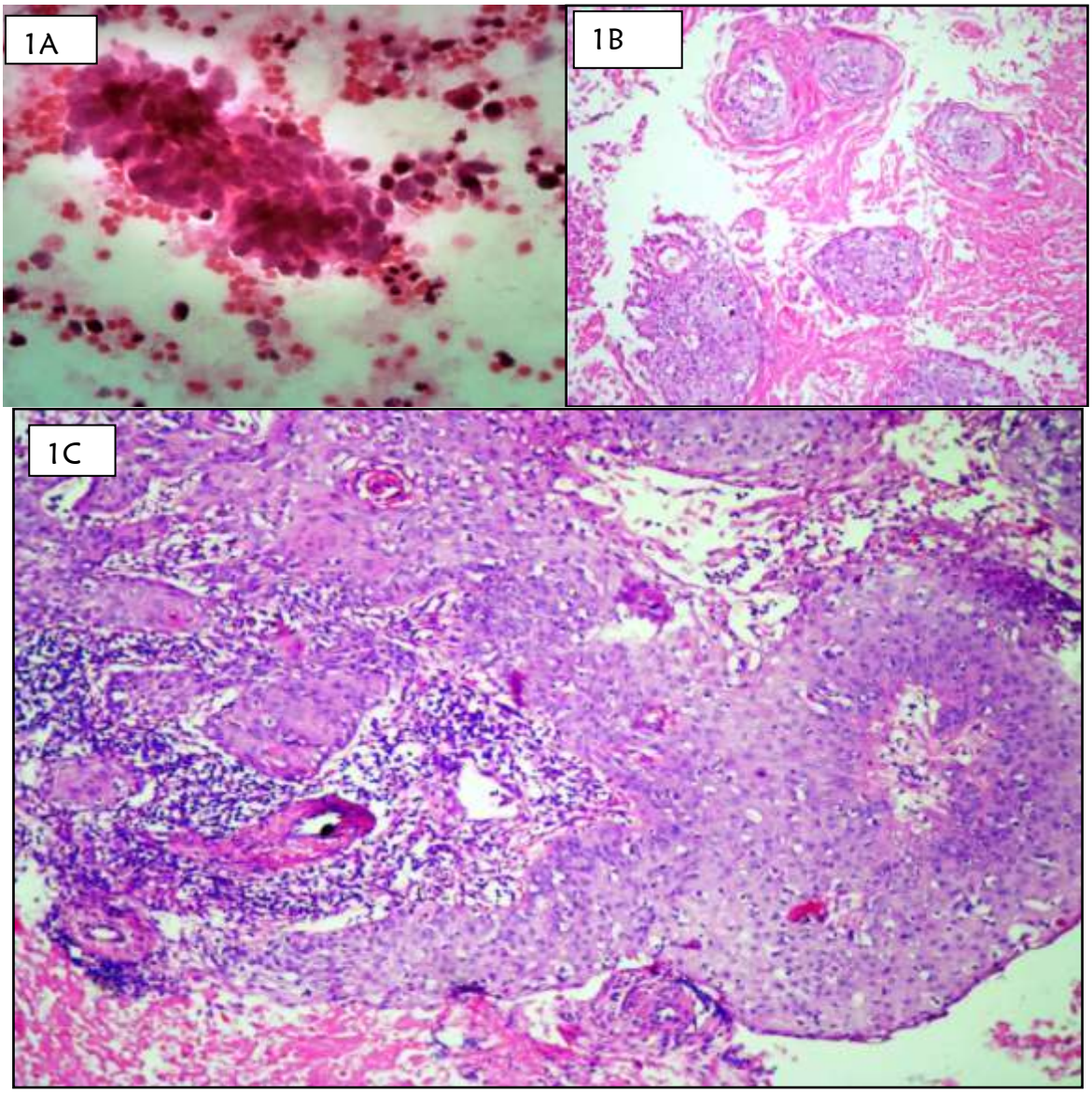
Volume 2, Issue 3, pp: 54-62 www.ijdmsrjournal.com ISSN: 2582-6018

PHOTOS



1A)Urine cytology- positive for malignant cells
1B)Squamous cell carcinoma with attempeted pearl formation (H &E)
1C) Squamous cell carcinoma

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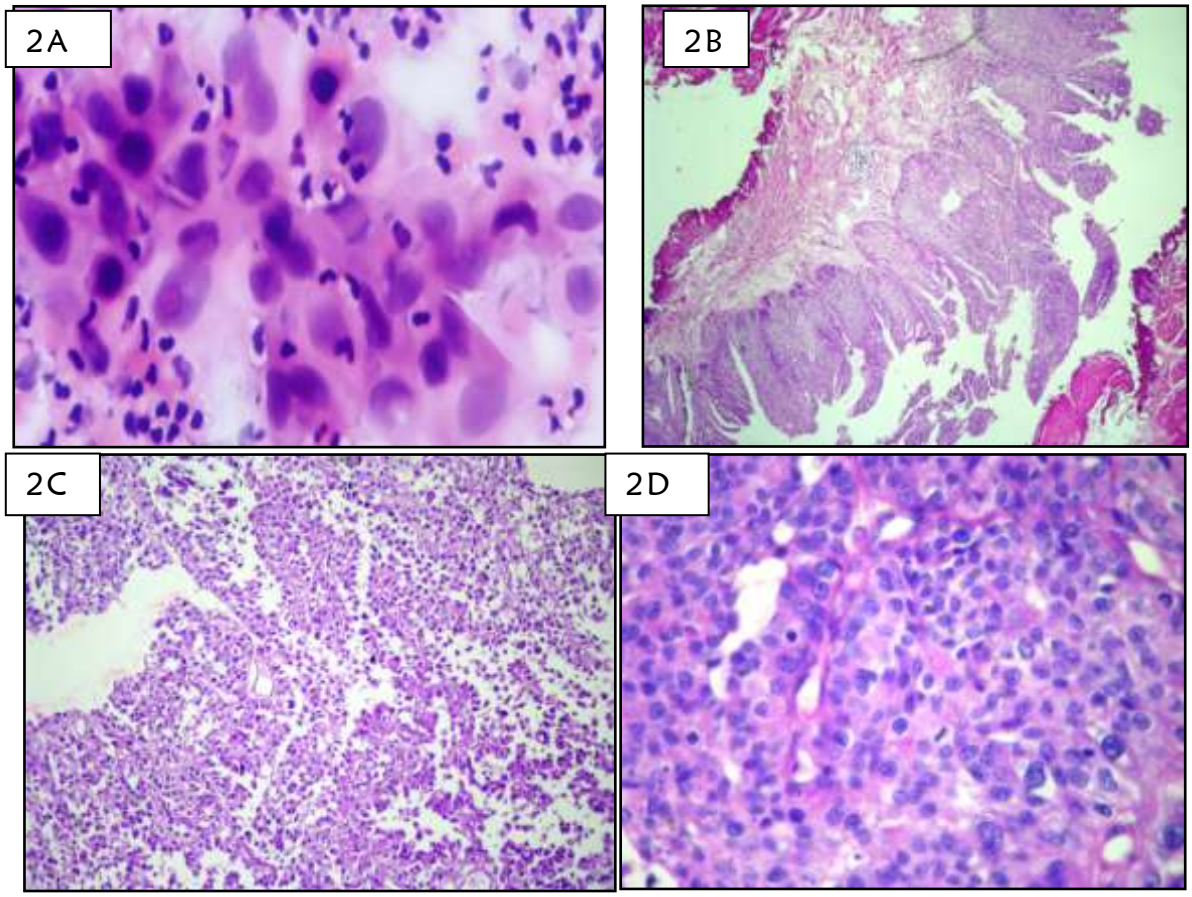
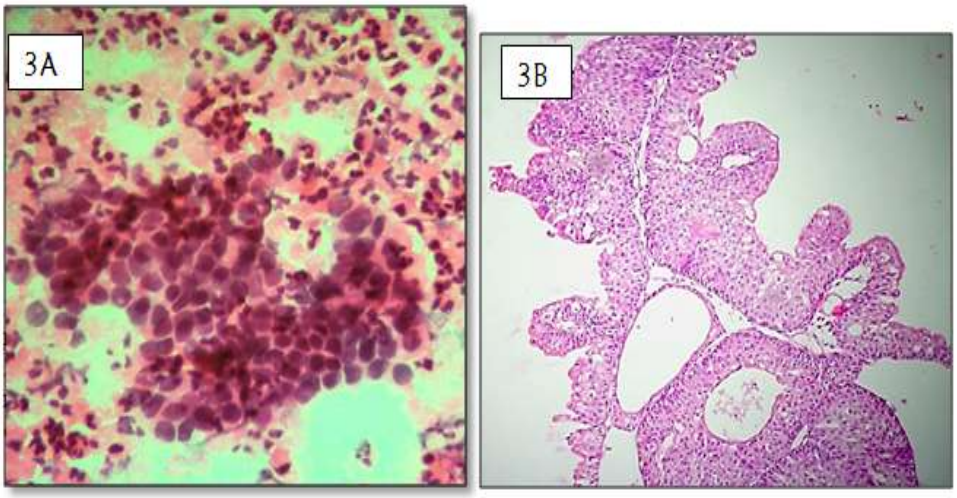


2A)urine cytology- positive for malignant cells
2B) High grade papillary urothelial neoplasm [HGPUN] (H & E)
2C)High Grade Papillary Urothelial neoplasia - showing dyscohesive tumor cells(H &E)
2D)High Grade Papillary Urothelial neoplasia with pleomorphic cells and mitotes in the upper layers (H & E)



3A) Urine cytology – Suspicious of malignanacy
3B) papillary urothelail neoplasm of low malignant potential [PUNLUMP] with delicate papillae (H&E)

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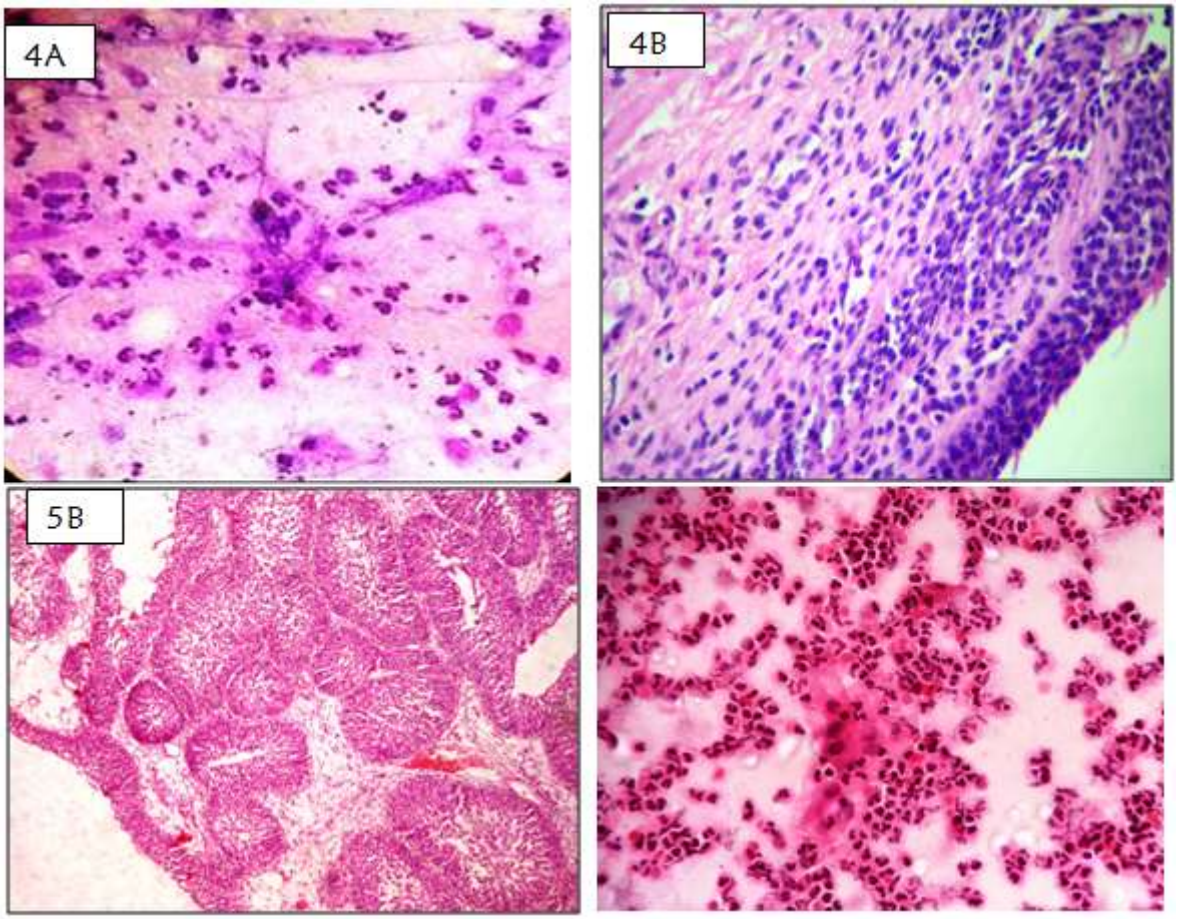
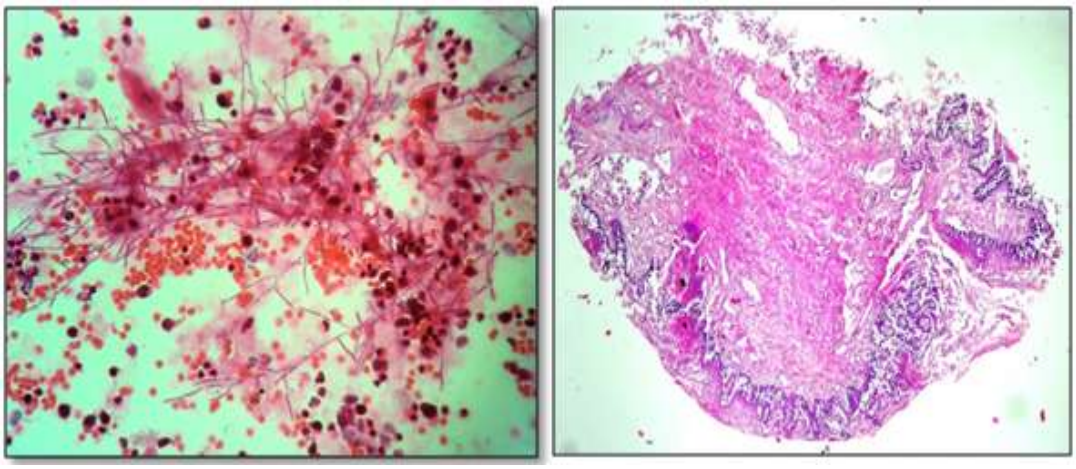


4A)urine cytology – inflammatory cells and few degenerated epithelial cells
4B)Chronic nonspecific cystitis with lymphoplasmacytic infiltrate sub epithileally(H&E)
5A) urine cytology – inflammatory cells and few atypical cells
5B) Inverted Papilloma (H &E)



6A) Urine cytology – inflammation with candida filaments
6B)Polypoidal cystitis (H &E)

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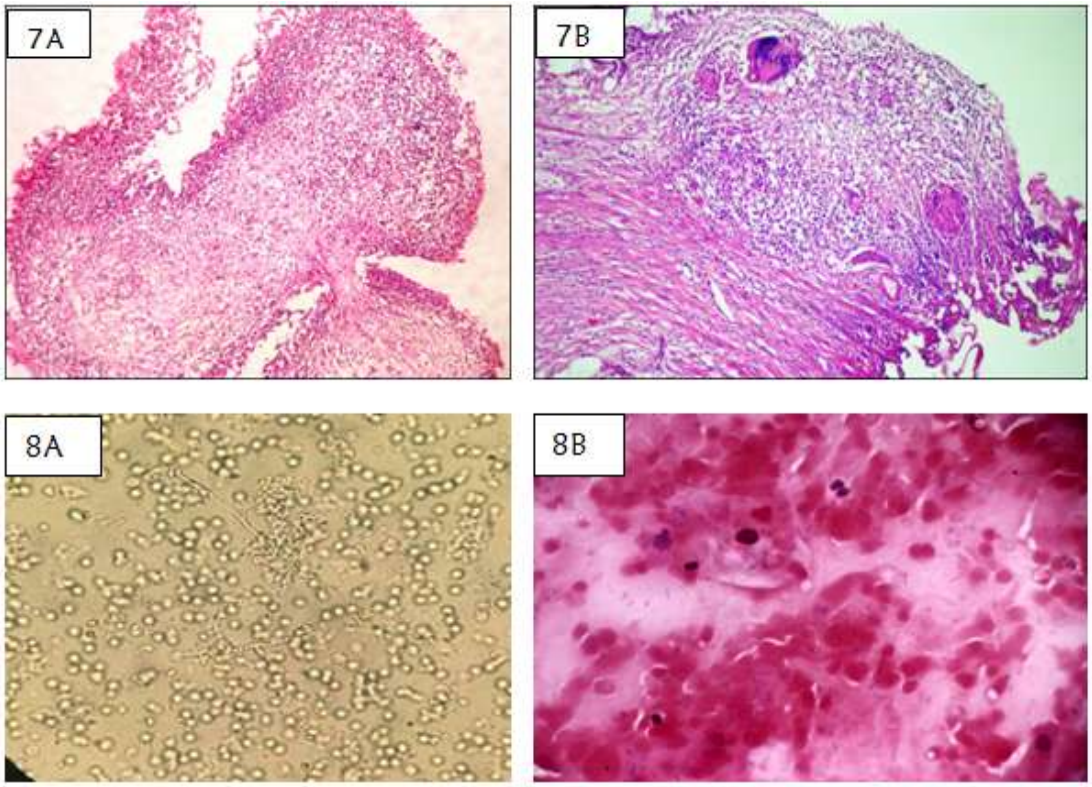

7A – HPE of the same case showing chronic nonspecific cystitis
7B – HPE showing Tuberculous cystitis with lymphocytes and langhnas type giant cells
8A,8B – urine cytology shows inflammatory cells and cadidial filaments

Tables

Table 1–Incidence of hematuria with age, sex and history of smoking in 290 cases

Characteristic	Cases Negative for atypical cells	Cases Positive for atypical cells
Male	173(59.6%)	28(9.67%)
Female	75(25.8%)	14(4.8%)
Age <40 years	127(43.7%)	11(3.8%)
Age >40 years	121(41.7%)	31(10.7%)
History Tobacco use	181(62.4%)	23(7.9%)
No history of tobacco use	67(23.1%)	19(6.6%)

Table 2 – cytology reports of 229 hematuria patients with negative for atypia

Test result	Number of cases	Number of cases (19 cases) follow up for histopathology
Inflammatory pathology	133(58.1%)	19/143
Non specific findings	76(33.1%)	00
Non contributory	20(8.7%)	00

Table 3 – Urine cytology reports of 51 hematuria patients with atypia

Test result	Number of cases positive in cytology	Number of cases (51 cases) follow up for histopathology	Number of cases diagnosed as malignant in histopathology
Malignancy	24(39%)	21/24	21
Suspicious of malignancy	18(29.5%)	15/18	6
Few atypical cells	19(31.1%)	15/19	2

Out of 61 cases 10 cases had inadequate biopsy specimen for reporting .