

AN ANALYSIS OF THE CLINICAL PRESENTATION, DIAGNOSIS, MANAGEMENT OPTIONS AND OUTCOME OF THE PATIENTS WITH GENITO-URINARY TUBERCULOSISA. Bhagavan¹, T. Jagadeeshwar², G. Ravichandar³, K. V. Narendra⁴**HOW TO CITE THIS ARTICLE:**

A. Bhagavan, T. Jagadeeshwar, G. Ravichandar, K. V. Narendra. "An Analysis of the Clinical Presentation, Diagnosis, Management Options and Outcome of the Patients with Genito-Urinary Tuberculosis". Journal of Evolution of Medical and Dental Sciences 2015; Vol. 4, Issue 46, June 08; Page: 7968-7976, DOI: 10.14260/jemds/2015/1159

ABSTRACT: AIMS AND OBJECTIVES: To analyze various clinical presentations and the treatment options in the management of the patients with genitourinary tuberculosis and to evaluate the role of urinary PCR in the detection of mycobacterium tuberculosis in patients with a clinical suspicion of genito urinary tuberculosis and to compare its sensitivity with urine for AFB smear, urine for myc. tuberculosis culture and bladder biopsy. **MATERIALS AND METHODS:** This is a retrospective and prospective study of patients with a diagnosis of genitourinary tuberculosis who underwent treatment in Gandhi General Hospital between January 2009 to December 2014. 62 patients with a diagnosis of genitourinary tuberculosis who underwent treatment were taken initially into the study. Five patients lost follow up after initial visits. These patients were excluded from the study. The remaining 57 patients were managed. **RESULTS:** Irritative voiding symptoms (Frequency / Urgency / Dysuria) were the most common symptoms. Gross hematuria seen in 22(38.5%) patients and microscopic hematuria seen in 53% of patients. Urine for AFB attaining was positive in 16(31.3%) patients, urine for MTb culture was positive in 21(41.1%) patients and pus for MTb culture was positive in 4 of 7 cases. Urinary PCR to identify the mycobacterial DNA was performed in 37 patients and was positive in 25(67.5%) of 37 clinically suspected cases. The urinary PCR was falsely positive in 1(2.7%) and falsely negative in 12(32.5%) patients. Kidney was involved in 26(45.6%) cases and ureter in 24(42.1%), and bladder in 28(49.1%) cases. Overall surgical intervention was done in 36 patients. All patients received 4 to 8 weeks ATT before they were taken up for surgical intervention. In 24 patients who presented with ureteric strictures, 7 patients had nonfunctioning kidneys and subsequently underwent nephroureterectomy, 8 patients had subnormal renal function in whom DJ stenting was done in 6 patients and PCN was done in 2 patients where DJ stenting was not possible. **CONCLUSION:** The manifestations of genitourinary tuberculosis can be variable and cause a variety of clinical patterns that mimic other diseases. Most of the cases present with advanced disease and high index of suspicion is necessary for the early diagnosis of genitourinary tuberculosis. PCR presents an advance in the diagnosis of GUTB. Urinary PCR is the most sensitive indicator of all microbiological tests and in combination with radiological abnormalities provides much faster diagnosis of genitourinary tuberculosis. However, it is an elaborate test that requires meticulous care to avoid false-positive and false-negative results. Multidrug chemotherapy combined with judicious surgery as and when indicated is the ideal treatment.

KEYWORDS: Genito Urinary Tuberculosis, Polymerase Chain Reaction, Anti Tuberculosis Treatment, Urinary Tract Infection.

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INTRODUCTION: Tuberculosis is a major public health problem with an estimated global incidence of 8-10 million per year and particularly in developing nations of Southeast Asia where nearly 3 million new cases and 700000 deaths occur in a year. Genitourinary tuberculosis is a relatively common form of extra pulmonary tuberculosis, constituting 10-14% of cases in developing countries.^(1,2,3)

Tuberculosis of the urinary tract is not uncommon in India, and it continues to be an important clinical problem, mainly because of its nonspecific clinical presentation and variable radiographic appearance which often mimic other pathological lesions. Early diagnosis of the disease allows administration of antitubercular treatment at a stage at which it may be curative.⁽³⁾ However, more often than not, the diagnosis is delayed because of a delay in presentation and in making a definitive diagnosis, with the consequence that a number of patients present with nonfunctioning kidneys, ureteral stricture, and shrunken bladder.^(4,5,6) These changes can be avoided if the diagnosis is made early and treated effectively.

AIMS AND OBJECTIVES: To analyze various clinical presentations and the treatment options in the management of the patients with genitourinary tuberculosis and to evaluate the role of urinary PCR in the detection of mycobacterium tuberculosis in patients with a clinical suspicion of genitourinary tuberculosis and to compare its sensitivity with urine for AFB smear, urine for myc. tuberculosis culture and bladder biopsy.

MATERIALS AND METHODS: This is a retrospective and prospective study of patients with a diagnosis of genitourinary tuberculosis who underwent treatment in Gandhi General Hospital between January 2009 to December 2014. 62 patients with a diagnosis of genitourinary tuberculosis who underwent treatment were taken initially into the study. Five patients lost to follow up after initial visits. These patients were excluded from the study. The remaining 57 patients were managed.

All patients are evaluated with detailed clinical history and physical examination, followed by a complete hemogram, renal function tests and liver function tests. Urine examination, including bacterial cultures was performed. Urine for AFB staining and mycobacterial cultures was obtained on first morning sample on 3 consecutive days. The first morning sample of urine was also sent for PCR for detection of mycobacterium tuberculosis in 37 cases.⁽⁷⁾

Radiological evaluation included chest x-ray, KUB in all cases and intravenous urogram when serum creatinine was normal. A micturatingcystourethrogram, nephrostogram and retrograde pyelogram, ultrasound study of abdomen and computerized tomography and MRI were obtained as and when necessary.⁽⁸⁾ Cystoscopy, bladder biopsy was done wherever indicated. FNAC was performed in cases with scrotal masses. Renal nuclear scans were done selectively to ascertain renal function in compromised kidneys.

All patients received antitubercular drug therapy with 4 drugs (Rifampicin, Ethambutol, Isoniazid and Pyrazinamide) for 2 months followed by 2 drugs (rifampicin and isoniazid) for 7 months.⁽⁹⁾ Temporary urinary diversion in the form of DJ stenting or PCN was performed in case of obstruction. The operative procedure was selected depending upon the organ involved, the extent of the disease, functional status of the involved organs and overall renal function. Tissue/organ removed were sent for histopathological examination.^(9,10,11)

Follow up included physical examination, complete hemogram, renal function tests and liver function tests and ultrasound KUB at 3, 6, 9 and 12 months. Follow up intravenous urogram, renal

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nuclear scan, cystogram were obtained at 3 months. In case of obstruction, renal nuclear scan was performed at 6, and 12 months. All the patients were followed up with 6 monthly RFT and ultrasound KUB region for 2 years and yearly RFT thereafter.

RESULTS: During the 5 year period, 62 cases of genitourinary tuberculosis were identified, out of which 5 patients were lost to follow up after initial visits and they were excluded from the study. The study included 39 males (68.4%) and 18 females (31.2%) with a ratio of 2:1. The age range was between 20 - 62 years and the mean age was 32.4 yrs.

Clinical Presentation: Irritative voiding symptoms (Frequency/Urgency/Dysuria) were the most common symptoms. Gross hematuria seen in 22(38.5%) patients and microscopic hematuria seen in 53% of patients, 15(26%) cases had pulmonary tuberculosis, and four of them had active disease at the time of diagnosis. The remaining clinical features are shown in the Table 1.

Sl. No.	Symptoms	No. of Patients
1	Frequency/urgency	41(72%)
2	Flank pain	19(33%)
3	Hematuria	22(38.5%)
4	Constitutional symptoms	18(31%)
5	Recurrent UTI	12(21%)
6	Scrotal mass	3(5.2%)
7	Penile ulcer	1(1.7%)

Table 1: Clinical Presentation

Laboratory Findings: Pyuria and hematuria with sterile urine culture was the most common urinary findings. However concurrent pathogens were cultured from urine in 12 patients (E. Coli in 8 cases, proteus in 2 cases enterobacter in 1 case) Klebsiella in 1 case). The remaining laboratory findings are shown in the Table 2.

Sl. No.	Lab Findings	No. of Patients
1	Anemia (<10gm %)	26(45.6%)
2	Poor renal function (Cr > 1.5mg %)	17(29.8%)
3	Leukocytosis(WBC> 11 000/mm ³)	11(19.2%)
4	Raised ESR	47(82.4%)
5	Positive Mantoux test	21(36.8%)
6	Pyuria(WBC> 10/ hpf)	32/57(56.1%)
7	Sterile urine	45/57(79%)
8	Positive AFB staining in urine	16/51(31.3%)
9	Positive MTb culture in urine	21/51(41.1%)
10	Positive MTb culture in pus	4/7(57.1%)
11	Positive PCR for MTb in urine	25/37(67.5%)

Table 2: Laboratory Findings

Urine for AFB attaining was positive in 16(31.3%) patients, urine for MTb culture was positive in 21 (41.1%) patients and pus for MTb culture was positive in 4 of 7 cases. Urinary PCR to identify the mycobacterial DNA was performed in 37 patients and was positive in 25(67.5%) of 37

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clinically suspected cases. The urinary PCR was falsely positive in 1 (2.7%) and falsely negative in 12(32.5%) patients.

PCR for detection of mycobacteria was also done in pus which was aspirated while doing Percutaneous Nephrostomy in cases of pyonephrosis and tissue from surgical specimen or bladder biopsy was sent for PCR for identification of mycobacteria.

A radiological abnormality (IVU/NCCT/MCUG) suggestive of GUTB was found 46(80.7%) cases. Bladder biopsy was positive in 12(48%) cases out of 25 cases done.

Comparison of urinary PCR with urine for AFB staining, urine for MTb culture and bladder biopsy was done as mentioned in the following Table 3.

PCR	Urine for AFB		Urine for MTB culture		Bladder biopsy	
	+ve	-ve	+ve	-ve	+ve	-ve
Positive	9	16	11	14	8	8
Negative	01	11	02	10	4	5

Table 3: Comparison of Urinary PCR with Urine for AFB Smear, Urine for MTb Culture, and Bladder Biopsy

Organ Involvement: Kidney was involved in 26(45.6%) cases and ureter in 24(42.1%), and bladder in 28(49.1%) cases. Radiological evidence suggestive of tuberculosis such as calcification, calyceal destruction, ureteral stricture, vesicoureteral reflux and small capacity bladder was apparent in 80.7% of cases. Cystourethroscopy was performed in 37 cases and stricture urethra was seen in 2 cases. Bladder had evidence of chronic cystitis in the vast majority of cases. Bladder biopsy was diagnostic in 12(48%) of 25 cases biopsied. FNAC was suggestive of tuberculosis in 3 cases of epididymitis. The results were summarized in Table 4.

Organ Involved	No. of Patients
Renal lesions	26
UPJ obstruction	2
Ureteral lesions	24
Upper ureter	2
Mid ureter	2
Lower ureter	14
Diffuse	6
Bladder	28
Chronic cystitis	19
Contracted bladder	9
Prostate	5
Epididymis	3
Seminal vesicles and Vas	2
Urethra	2
Complex lesions (more than 3 sites)	9

Table 4: Organ Involvement

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Surgical Intervention: Overall surgical intervention was done in 36 patients. All patients received 4 to 8 weeks ATT before they were taken up for surgical intervention. In 24 patients who presented with ureteric strictures, 7 patients had nonfunctioning kidneys and subsequently underwent nephroureterectomy, 8 patients had subnormal renal function in whom DJ stenting was done in 6 patients and PCN was done in 2 patients where DJ stenting was not possible. In these 8 patients who had poor renal function, 5 patients had worsening of the function and subsequently underwent nephroureterectomy. The remaining 3 patients had regular change of DJ stent while on ATT for 9 months and 1 patient underwent ureteral dilatation after DJ stenting for 1 year and their renal function have improved. 4 patients underwent ureteroneocystostomy in the form of psoas hitch in 3, and boari flap reconstruction in 1 patient. Ilealureter replacement was done in 2 patients. Ureteroureterostomy was done in 2 patients who had single stricture with less than 2 cm length. The other performed surgical procedures were shown in the table 5.

Surgery	No.
Nephrectomy/nephroureterectomy	12
Pyeloplasty	1
Ureteral reconstruction	8
Ureteroureterostomy	2
Psoas hitch	3
Boari flap	1
Ileal ureter	2
Augmentation cystoplasty	9
Ileocystoplasty	6
Sigmoid colocolocystoplasty	2
Ileocystoplasty + ileal ureter	1
Epididymectomy	3
Visual internal urethrotomy	2
Table 5: Surgical Intervention	

Augmentation cystoplasty was performed in 9 patients and bladder capacity improved significantly in all patients. 1 patient underwent ileocystoplasty along with ileal ureter replacement and his renal function has improved in the follow up period.

All patients were followed up regularly at 2 weeks, 3 months and 6 months after discharge, and every 6 months thereafter. Follow up ranged from 3 months to 5 yrs. 1 patient died of renal failure and sepsis following surgery for renal stone. Renal function improved in 22 patients, stabilized in 12 and worsened in 6 patients.

DISCUSSION: Tuberculosis can involve any organ system in the body and produce protean manifestations. The most common presenting symptoms in patients of genitourinary tuberculosis are irritative voiding symptoms and hematuria in 60% and 50% cases respectively^(12,13). In our series irritative voiding symptoms were seen in 41(72%) cases, hematuria in 22(38.5%) and constitutional symptoms in 18(31 %) cases. Of our patients 12(21 %) had recurrent urinary tract infection. The incidence of renal failure in our series was 29.8% is comparable to that reported in the literature,^(12,13) (24%).

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Mycobacterium was grown in urine culture in 41.1% of our cases as compared with 50 to 90% reported in the literature. The low detection rate in our cases was probably due to incomplete and intermittent treatment by primary care physicians for tuberculosis in the past. Radiological abnormalities in genitourinary tuberculosis are reported in 63% to 95% of cases.⁽¹⁴⁾ We found such evidence in 80.7% of our cases. The common radiological abnormalities seen were calcification, cortical scarring, calyceal destruction, nonvisualized kidney, ureteral stricture or irregularity and contracted bladder. This high percentage may be due to late presentation of the cases. We performed bladder biopsy in 25 cases to aid in the diagnosis and positive yield was obtained in 12 cases (48%). Wong et al,⁽⁹⁾ achieved a tissue diagnosis in 18.5% of their cases and reported no adverse effects of bladder biopsy. However Gow,⁽¹⁵⁾ suggests bladder biopsy should not be carried out unless a malignancy needs to be excluded.

PCR is a technique that can be used to amplify a specific DNA genomic sequence, whereby the presence of an extremely small number of bacteria can be detected.⁽¹⁶⁾ The high sensitivity of PCR is particularly useful in paucibacillary situations. PCR can provide much faster confirmation of the diagnosis (24-48 hrs) than MTb culture.⁽¹⁷⁾ The limit of detectability of PCR may vary from about 10 organisms to as little as 1 bacillus. Urinary PCR is specific for the MTb complex (MTb and *M. bovis*) and no crossover reaction occurs with other mycobacteria. In the 37 cases of proven GUTB where PCR was done, it was positive in 25 (67.5%) cases which is low when compared with other studies in the range of 85% to 95%. In this study urinary PCR is falsely positive in 1 case (2.7%) and it may be caused by contamination due to the presence of amplicons or MTb complex bacilli or DNA. False-negative results are found in 32.5% of the samples in our study in contrary to 5-15% reported in the literature. False-negative findings may result from the presence of inhibitors; nonhomogeneous distribution of bacteria in the specimen so that the fraction tested does not contain mycobacteria; or low numbers of mycobacteria in the specimen, which decreases the probability of the presence of organisms in the fraction analyzed by PCR.^(16,18) In our study the sensitivity of Urinary PCR is high (67.5%) when compared to the sensitivities of urine for AFB staining (31.3%), MTb culture (41.1%) and bladder biopsy (48%).⁽¹⁷⁾

Modern antitubercular chemotherapy remains the cornerstone of management of genitourinary tuberculosis. Gow,⁽¹⁹⁾ has recommended short course chemotherapy of 6 months as there are fewer bacilli in renal lesions than in pulmonary ones, high concentrations of rifampicin are achieved in urine and there is good penetration of streptomycin and isoniazid into cavities. While this short course chemotherapy is also recommended by the WHO for uncomplicated extrapulmonary tuberculosis, a large number of our patients had received intermittent, incomplete antitubercular therapy before presenting to us.⁽¹⁹⁾ To ensure maximal chances of cure, we preferred to treat genitourinary tuberculosis as a complicated tuberculous infection with chemotherapy for at least 9 months.

The role of surgery is complimentary to antitubercular chemotherapy. A minimum of 4 weeks of ATT is recommended before any surgical intervention. This period allows stabilization of the lesion and better planning of the conservative or reconstructive surgery. In patients with compromised renal function due to obstruction, this period also aids recovery of renal function if adequate temporary urinary diversion is provided. We performed 26 nephrectomies including 12 nephroureterectomies for concomitant ureteral lesions. Of these patients 2 had nephrocutaneous fistula. Involvement of the renal parenchyma is often irreversible even with adequate chemotherapy. However not all patients with azotemia at presentation have irreversible renal damage.

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Tuberculosis may result in compromised renal function, unilaterally or bilaterally, due to obstruction at the at the ureteropelvic junction or due to ureteral or urethral strictures. These conditions are amenable to renal salvage if early intervention in the form of temporary diversion is instituted along with ATT. Once the lesions stabilized a decision regarding definitive management can be taken. Discrete lesions can be managed initially with minimally invasive endoscopic procedures. If they fail, open surgery may be offered according to the merits of the case.

Reconstructive surgery for genitourinary tuberculosis is required in cases with a grossly distorted and dysfunctional anatomy that is unlikely to regress with chemotherapy alone.^(20,21,22) Earlier, reconstructive surgery was performed in about 10% of cases of advanced genitourinary tuberculosis but has increased to about 56% in recent times.⁽²³⁾ In this study we performed 46 surgical procedures and of these 18(38.2%) were reconstructive. Various bowel segments have been used in the process of reconstruction. We have used ileum and sigmoid colon and both segments produced equivalent results in terms of increase in functional capacity. Problems of dysuria and mucus discharge regressed significantly after a year and did not pose much of a problem thereafter.

CONCLUSION: The manifestations of genitourinary tuberculosis can be variable and causes a variety of clinical patterns that mimic other diseases. Most of the cases present with advanced disease and high index of suspicion is necessary for the early diagnosis of genitourinary tuberculosis.

PCR presents an advance in the diagnosis of GUTB. Urinary PCR is the most sensitive indicator of all microbiological tests and in combination with radiological abnormalities provides much faster diagnosis of genitourinary tuberculosis. However, it is an elaborate test that requires meticulous care to avoid false-positive and false-negative results.

Multidrug chemotherapy combined with judicious surgery as and when indicated is the ideal treatment. All attempts must be made to reconstruct the urinary tract as the results are gratifying. However, infected and destroyed tissue is best ablated.

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FINANCIAL OR OTHER

COMPETING INTERESTS: None

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Date of Submission: 15/04/2015.
Date of Peer Review: 16/04/2015.
Date of Acceptance: 30/04/2015.
Date of Publishing: 05/06/2015.