



A study on etiology, clinical presentation and management of genitourinary tuberculosis: A prospective study

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Abstract

Background: Genitourinary tuberculosis (GUTB) is the second most common form of extrapulmonary tuberculosis, with more than 90% of cases occurring in developing countries. In GUTB, the kidneys are the most common sites of infection and are infected through hematogenous spread of the bacilli, which then spread through the renal and genital tract. **Aim & Objectives:** The main aim of the present study is to identify the etiology, clinical presentation and management of genitourinary tuberculosis.

Methodology: This is a prospective study of patients with a diagnosis of genitourinary tuberculosis who underwent treatment in Nizam's institute of medical sciences between September 2016 to December 2017. 60 patients with a diagnosis of genitourinary tuberculosis who underwent treatment were taken initially into the study.

Results: During this 18 months period, 60 cases of genitourinary tuberculosis were identified. The study included 19 males (70.37%) and 8 females (29.62%) with a M: F ratio of 2.3:1. The mean age of the patients was 33.74 years (range 17 to 54 years). The youngest patient in this study was 16 years old and the oldest patient was 56 years old. 2 patients were <20yr, 25 patients were between 21-30 yrs, 17 patients were between 31-40 yrs, 11 patients were between 41-50 yrs and 2 were above 50 yrs. Irritative voiding symptoms were the most common symptom seen in 38 cases (66.66%) followed by Flank pain in 19 cases (33.33%), hematuria in 14 cases (24.56%), recurrent UTI in 14 cases (24.56%), constitutional symptoms in 17 cases (29.82%), and scrotal mass in 4 cases (7.01%). In our study, Raised ESR was present in 36 patients (63.15%) followed by Sterile Pyuria in 35 cases (61.40%). Anemia was found in 25 cases (43.85%), raised serum creatinine in 20 cases (35.08%). Mantoux test was positive in 11 cases (19.29%) and Leukocytosis was present in 10 cases (17.54%). Overall surgical intervention was done in 49 patients. All patients received 4 to 8 weeks ATT before they were taken up for surgical intervention.

Conclusion: The study concluded that, all patients were followed up regularly at 2 weeks, 3 months and 6 months after discharge, and every 6 months thereafter. Renal function improved in 16 patients, stabilized in 30 and worsened in 9 patients. Although the role of surgery in GUTB has decreased since the advent of anti-TB therapy, it can still have a role as an adjunct to drug treatment. Today, the challenges of GUTB and other forms of TB include increasing rates of drug-resistant cases and co-infection with HIV.

Keywords: genitourinary tuberculosis, haematuria, creatinine, drug-resistant

Introduction

Tuberculosis (TB), a disease that is the cause of unaccountable human suffering and economic loss, paradoxically is to be considered a model disease as far as the scientific understanding of the disease *per se* is concerned. It is one of the earliest human afflictions for which a definitive cause was discovered.

Multidrug-resistant (MDR) TB is often associated with poorly managed pharmacotherapy, particularly in middle-income countries. The incidence of MDR TB is increasing and is of global concern.¹ Genitourinary TB (GUTB) is the second most common form of extrapulmonary TB (EPTB), after lymph node TB^{1, 2}. GUTB has the propensity to affect both men and women of child-bearing age (that is, 20–40 years old), is responsible for extensive morbidity and can render patients infertile. The nonspecific presentation of GUTB can result in delayed diagnosis and management of the disease, which could worsen morbidity. The mainstay of

GUTB treatment is antimycobacterial chemotherapy, and surgical intervention is reserved for patients with complications such as recurrent infections in a nonfunctioning kidney. In many developing countries, directly observed therapy has been successfully employed to ensure compliance with treatment and reduce the risk of drug resistance

Notwithstanding these distinctions, it is a sad fact that TB continues to be a major killer even today. In the present study, we focus on the etiology, clinical findings and medical treatment of TB in general and also focus on the aspects of treatment specific to the management of genitourinary TB (GUTB).

Materials and Methods

Place of the study & Duration

This is a prospective study of patients with a diagnosis of genitourinary tuberculosis who underwent treatment in

Nizam's institute of medical sciences between September 2016 to December 2017.

Study Population

60 patients with a diagnosis of genitourinary tuberculosis who underwent treatment were taken initially into the study. 3 patients were lost to follow up after initial visits. These patients were excluded from the study.

Inclusion criteria

- All the patients reporting to the hospital with proven genitourinary tuberculosis or diagnosed after coming to the hospital and were treated as inpatients were included in the study.

Exclusion criteria

- Patients who were not admitted to the hospital were excluded from the study.
- Patients with less than 6 months of follow up were also excluded from the study

History, physical examination, laboratory and radiological investigations were done on the patients, and the primary focus of the disease and the organs involved were determined. All the patients received treatment as indicated. The laboratory investigations done included urinalysis, full blood count with estimation of erythrocyte sedimentation rate (ESR), RFT, Mantoux (tuberculin) skin test, and screening for HIV.

Radiological evaluation included Chest X-ray, X-ray Kub & Ultrasound KUB in all cases. CT scan was done in most of the cases. IVU was done in some cases.

Treatment

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 4 months. 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 HPE

Follow up was done at 3,6,12 months with LFT, RFT, 3 early morning samples for AFB, USG. In case of obstruction, renal nuclear scan was performed at 6 and 12 months.

Observations and Results

During this 18 months period, 60 cases of genitourinary tuberculosis were identified, out of which 3 patients were lost follow up after initial visits and they were excluded from the study.

Table 1: Shows Sex distribution

Gender	Frequency	Percentage
Male	39	68.42%
Female	18	31.57%

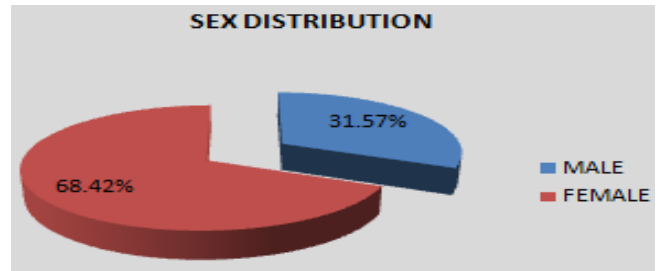


Fig 1: Shows Sex distribution

The study included 19 males (70.37%) and 8 females (29.62%) with a M: F ratio of 2.3:1.

Table 2: Shows Age distribution

Age group (in years)	Frequency	Percentage
<20	2	3.50%
21-30	25	43.85%
31-40	17	29.82%
41-50	11	19.29%
>50	2	3.50%

The mean age of the patients was 33.74 years (range 17 to 54 years). The youngest patient in this study was 16 years old and the oldest patient was 56 years old. 2 patients were <20yr, 25 patients were between 21-30 yrs, 17 patients were between 31-40 yrs, 11 patients were between 41-50 yrs and 2 were above 50 yrs.

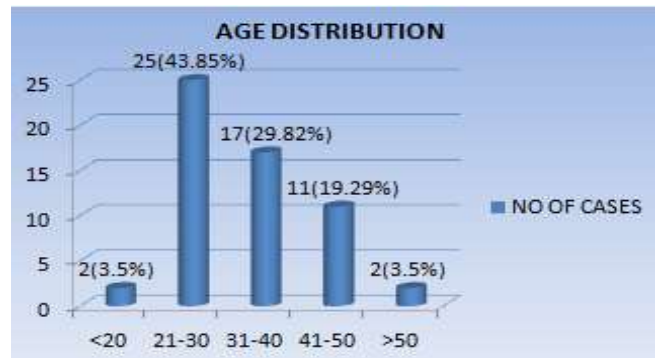


Fig 2: Shows Age distribution

Table 3: Symptoms and Signs

Symptoms and signs	Frequency	Percentage
Irritative voiding symptoms	38	66.66%
Flank/Loin pain	19	33.33%
Hematuria	14	24.56%
Recurrent UTI	14	24.56%
Constitutional symptoms	17	29.82%
Scrotal mass	4	7.01%

Irritative voiding symptoms were the most common symptom seen in 38 cases (66.66%) followed by Flank pain in 19 cases (33.33%), hematuria in 14 cases (24.56%), recurrent UTI in 14 cases (24.56%), constitutional symptoms in 17 cases (29.82%), and scrotal mass in 4 cases (7.01%). Past h/o pulmonary TB was present in 6 patients (10.52%).

Table 4: Shows Laboratory Findings

Lab Findings	Number of patients	Percentage
Anemia (< 10 gm.%)	25	43.85%
Poor renal function (Cr > 1.5mg %)	20	35.08%
Leukocytosis (WBC> 11,000/mm3)	10	17.54%
Raised ESR	36	63.15%
Positive Mantoux test	11	19.29%
Sterile Pyuria (WBC > 10/ hpf)	35	61.40%

In our study, Raised ESR was present in 36 patients (63.15%) followed by Sterile Pyuria in 35 cases (61.40%). Anemia was found in 25 cases (43.85%), raised serum creatinine in 20 cases (35.08%). Mantoux test was positive in 11 cases (19.29%) and Leukocytosis was present in 10 cases (17.54%).

All the patients were screened for HIV and none in our study were positive for HIV.

Table 5: Surgical procedures done in our study

Surgery	No. of cases	Percentage
Nephrectomy	14	24.56%
Pyeloplasty	1	1.75%
Ureter reimplantation with Psoas hitch	4	7.01%
Ureteric reimplantation with boari flap	4	7.01%
Augmentation cystoplasty and ureter reimplantation	3	5.26%
Augmentation cystoplasty Ileal conduit	15	26.31%
Ileal conduit with nephrectomy	2	3.50%
Ileal conduit with nephrectomy	2	3.50%
Visual Internal Urethrotomy	4	7.01%
DJ Stenting	4	7.01%
PCN	16	28.07%
Only Medical Mx (on ATT)	4	7.01%

Overall surgical intervention was done in 49 patients. All patients received 4 to 8 weeks ATT before they were taken up for surgical intervention. Out of the 49 patients, 14 patients had non-functioning kidneys and subsequently underwent nephrectomy. 20 patients had subnormal renal function in whom DJ stenting was done in 4 patients and PCN was done in 16 patients where DJ stenting was not possible. In these 20 patients who had poor renal function, 14 patients had worsening of the function and subsequently underwent nephrectomy. The remaining 6 patients had regular change of DJ stent while on ATT for 9 months. Ileal conduit was done in 4 patients. Augmentation cystoplasty was done in 15 patients of contracted bladder. Out of the 15 patients, 3 patients underwent simultaneous ureteric reimplantation also. Pyeloplasty was done in 1 case. 4 patients underwent ureteroneocystostomy in the form of psoas hitch. 4 patient’s undergone ureteric reimplantation with boari flap. Visual internal urethrotomy was done for

stricture urethra in 4 patientst. 4 patients were managed with ATT alone

All patients were followed up regularly at 2 weeks, 3 months and 6 months after discharge, and every 6 months thereafter. Renal function improved in 16 patients, stabilized in 30 and worsened in 9 patients.

Discussion

Tuberculosis can involve any organ system in the body and produce protean manifestations. Genitourinary TB accounts for 30% to 40% of all extra pulmonary TB. In developed countries, GUTB has been found in 2% to 10% of patients with pulmonary TB. In contrast the frequency in developing countries approaches 15% to 20% [3, 4].

Gender distribution

GUTB is more common in males than in females. In the study of Benchekroun *et al.* [5] (1998) 80 patients with GUTB were analyzed between 1985 and 1995. These patients consisted of 50 males (62.5%) and 30 females (37.5%). Some other authors have also found that GUTB affects more men than women others exactly the contrary [6]. It have been seem GUTB, as any other kidney disease, should be more often in female patients, because menses, gravidity, inflammation of genitals may hinder the urine passage. Urinary stasis makes the possibility for fixation of MBTB to urothelium, and, so, for developing renal TB. In the study of S. Ray *et al.* [7] (2012) of 40 patients, 30 were females and 10 were males. There were 38 males and 22 females with a mean age of 32.5 years in a study done by Bansal *et al* [8]. In our study, 39 were males (68.42%) and 18 were females (31.57%). The Male: Female ratio was 2.3: 1. The general health and nutritional status of TB-infected persons affects their rate of progression to disease. In areas where women’s health is less cared than men’s (especially in terms of nutrition), women’s risk of disease may be increased. A number of studies suggest that responses to illness differ in women and men, and that barriers to early detection and treatment of TB vary (and are probably greater) for women than for men [9].

Table 6: Studies investigating M/F ratio in GUTB

Study	Males	Females	Male: female Ratio
Benchekroun <i>et al.</i> (1998) [5]	50	30	1.66:1
S. Ray <i>et al</i> [7]. (2012)	10	30	1:3
Bansal <i>et al</i> [8] (2015)	38	22	1.72
Current study	39	18	2.1:1

Age Distribution

Genitourinary tuberculosis is a disease of the young adults. In our study 73.67% of the patients are between the ages of 20 and 40. In the study of Benchekroun *et al* [5] (1998) the mean age of the patients was 38 yrs (range 20 – 50 yrs). In the study of Orakwe. J.C *et al.* [10] (2005) the mean age of the patients was 37.6 yrs (range of 20 – 60 yrs) with preponderance of the cases in the third and fourth decades. In the study of Smita Chandra *et al.* [11] (2012) mean age of presentation was 37.7 years. In our study the mean age of the patients was 33.74 years (range 16 to 56 years) which was consistent with the findings of above studies. The youngest patient in our study was 16 years old and the oldest patient was 56 years old. 2 patient was <20yr, 25 patients were between 21-30 yrs, 17 patients were between

31-40 yrs, 5 patients were between 41-50 yrs and 2 was above 50 yrs. In our study majority of patients (42 cases, 73.67%) were between 21 to 40 yrs which was consistent with the findings in the above studies. The most common mode of transmission to the genitourinary tract is through hematogenous spread from pulmonary or other sites of tuberculosis. Genitourinary tuberculosis is a chronic disease and often has low-grade symptomatology with very few specific complaints.

Table 7

Study	Mean Age
Benchekrroun <i>et al.</i> (1998) [5]	38 yrs
Orakwe. J.C <i>et al.</i> (2005) [10]	37.6 yrs
Smita Chandra <i>et al.</i> (2012) [11]	37.7 yrs
Current study	33.74 yrs

Clinical features

Genitourinary tuberculosis raises major diagnostic problems due to the frequently atypical and misleading clinical features. Human infection is mainly caused by Mycobacterium Tuberculosis and M. Bovis. Immunity is predominantly mediated by T-helper cells, cytokines and the genetic makeup of the host. GUTB may occur as a secondary infection due to decreased cellular immunity (Lenk *et al.*, 2011) [12]. Immunosuppression may be due to malnutrition, acquired immunodeficiency or extreme age. Possible modes of spread to the genitourinary organs included direct extension, hematogenous spread and descending infection (Eastwood *et al.* [53]) Testicular involvement by hematogenous spread and venereal transmission is rare. A high index of suspicion should be maintained in patients with HIV infection, post-transplant patients, children with nephrotic syndrome and cases of vitamin D deficiency. It is a serious disease as the lesions are often multifocal and extensive, requiring major surgical resection and urinary tract reconstruction [3, 13, 7]. Diagnosis is often difficult because TB has a variety of clinical findings. It can mimic numerous other disease entities. A high level of clinical suspicion allows early diagnosis and

timely initiation of proper management [13]. The nonspecific clinical features of GUTB make the early and accurate diagnosis of the disease difficult. The most common presenting symptoms in patients of genitourinary tuberculosis are irritative voiding symptoms and hematuria in 60% and 50% cases respectively [14, 15]. In our series irritative voiding symptoms were seen in 38(66.66%) cases, hematuria in 14(24.56%) and constitutional symptoms in 17(29.82 %) cases. Of our patients 14(24.56%) had recurrent urinary tract infection. The incidence of renal failure in our series was 35.08%, comparable to that reported in the literature of 24% [14, 15]. In review of 8961 cases by Figueiredo *et al.* [16] from the world literature a great difference was shown between clinical features of GUTB in different regions depending on epidemic situation, advancing of country etc. [16].

In the 10 year experience of Kao *et al.* [17] (1996) 89% percent of the patients had abnormal urinalysis: hematuria and/or pyuria. Urinalysis is the least invasive method of diagnosing GUTB. The classically described —sterile pyuria is not very sensitive or specific for GUTB, but persisting sterile pyuria in an individual at risk should increase the clinician’s index of suspicion [17].

In the study of el Khader *et al.* [18] (2001) irritative voiding symptoms were the most frequent (47.3%). Constitutional symptoms were rare (11%). 16% of patients had an isolated genital lesion.

In the study of 131 GUTB patients by Kulchavenya *et al.* [19] (2013) flank pain was seen in 35.2% and dysuria was seen in 39.8%, 9.1% had renal colic, and 7.9% had gross hematuria. Sterile pyuria was seen in 25% only. In our study sterile pyuria was seen in 61.40%. Irritative voiding symptoms, flank pain and sterile pyuria are seen in higher percentage of cases in our study probably due to late presentation and diagnosis of the cases at a severe stage. The usual constitutional symptoms such as fever, weight loss, and night sweats were reported in 29.82% of our cases. A varied incidence of these symptoms (ranging from 5-20%) has been reported in several such studies [20]

Table 8

Symptoms and signs	Kader <i>et al.</i> [18](2001)	Kulchavenya <i>et al.</i> [19] (2013)	Smita Chandra <i>et al.</i> [11] 2012	Current study
Irritative voiding symptoms	47.3%	39.8%	56%	66.66%
Flank pain	---	35.2%	56%	33.33%
Sterile pyuria	---	25%	40%	61.40%
Hematuria	---	7.9%	44%	24.56%
Constitutional symptoms	11%	17%	32%	29.82%

Treatment

Medical therapy

Anti-tuberculous drug treatment is based on an initial 2 month intensive phase with three or four drugs daily followed by a 4 month continuation phase with only two drugs [13]. In epidemic regions GUTB used to be treated with four or five drugs for 8-12 months [13]. WHO recommended reducing the treatment time to nine or six months with 4 drugs (isoniazid, rifampicin, pyrazinamide and streptomycin or ethambutol); in complicated or complex cases the length of the therapy may be 12-14 months. In cases of re-treatment, immunosuppression and HIV/AIDS the treatment time increases to nine or 12 months. In this study only 4 patients were advised 6 months of ATT, rest of the patients were advised 9-12 months of ATT as the patients presented

in late stage with severe form of the disease. Those patients who were diagnosed solely on the basis of histopathology of the operative specimen started ATT post operatively.

Surgical therapy

Chemotherapy for late-diagnosed complicated forms of GUTB is not enough effective, so surgery is indicated. Surgery was required in 32% of cases in the study done by Smita Chandra *et al.* [11], showing delayed diagnosis leads to more destruction of organs requiring surgical intervention. The organ-removing operations were conducted in 73% of patients. In our study, 16 cases (28.07%) underwent organ removing operations which included 14 nephrectomies and in 2 patients ileal conduit with nephrectomy was done. In a study done by Dilip kumar *et al.* [21], nephrectomy was done

in 28.57%, In our study percutaneous nephrostomy was done in 16 cases before proceeding with nephrectomy/augmentation cystoplasty and ureter reimplantation /ileal conduit. Urinary bladder rehabilitation by augmentation cystoplasty increases the bladder capacity and storage time and also preserves the upper tracts ²². In our study augmentation cystoplasty was done in 18 cases (31.57%) and ileal conduit was done in 6 cases with contracted bladder who had renal failure. In a study done by Dilip Kumar et al ^[21], ileocystoplasty was done in 28.57%, Stenosis of the ureter usually can be managed by temporary stenting and adjuvant corticosteroid therapy which if unsuccessful might need a ureteral reconstruction. In our study DJ stenting was done in 2 cases, ureter reimplantation with psoas hitch in 5 cases (18.51%). Some researchers advocate that surgical intervention should only be performed 4 weeks after the initiation of TB treatment, but there is no evidence to support this idea ^[23]. Other investigators suggest that patients should be treated with anti-TB drugs for at least 6 months before reconstructive surgery is performed. Interestingly, a 10-year study of 101 patients with confirmed GUTB from Korea showed that more than 50% of these patients required surgical intervention in addition to medical treatment ^[24]. Insidiousness of onset and difficulty in diagnosis may lead to a delay in treatment. This may result in serious complications such as the destruction of kidney or severe involvement of the urinary bladder. Surgery continues to play a role in the management of GUTB, despite the availability of effective ATT ^[8]. In the recent past, there has been a tremendous increase in the variety of reconstructive procedures for the urinary bladder, used in the management of GUTB ^[25]. Timely diagnosis and treatment will prevent the late sequelae of this disease, like nonfunctioning kidney and thimble urinary bladder. Augmentation cystoplasty includes the goals of increasing bladder capacity, while retaining as much of the bladder as possible. All patients were followed up regularly at 2 weeks, 3 months and 6 months after discharge, and every 6 months thereafter. Renal function improved in 16 patients, stabilized in 30 and worsened in 9 patients.

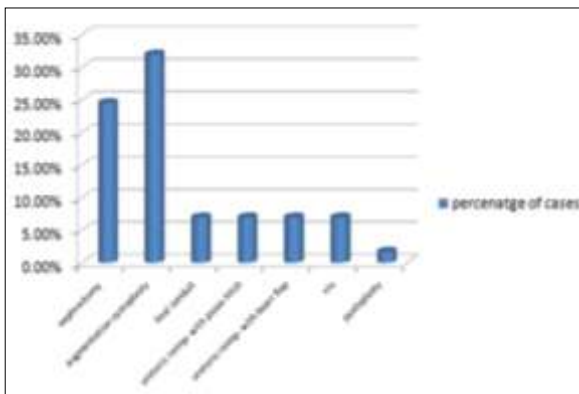


Chart 9: Surgical Procedure Done



Images 1: Thimble bladder with left non functioning kidney – augmentation cystoplasty with left nephrectomy

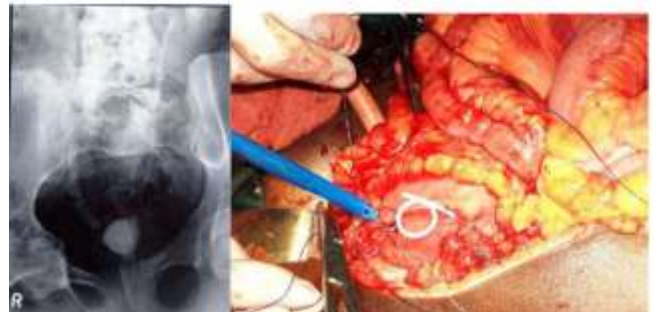


Image 2: contracted bladder with diverticulum with It vuj stricture – ileocystoplasty with It ureteric reimplantation

Conclusion

CT is replacing IVU as an imaging modality of choice in GUTB. Antitubercular therapy is the mainstay of treatment. Genitourinary tuberculosis results in sequelae which may require major organ removing and reconstructive surgeries. 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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Conflict of interest

The author declare that, they have no conflict of interest
Ethical clearance taken from Institutional ethical committee.

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