

Genitourinary tuberculosis: clinical profile, diagnostic approach and treatment outcome in a tertiary care center of North India

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Abstract

Introduction: Genitourinary tuberculosis (GUTB) is the second commonest form of extrapulmonary tuberculosis with more than 90% of cases occurring in developing countries and kidney being the most common site of involvement. We present clinico-epidemiological profile of patients and management of genitourinary tuberculosis in IGMC Shimla. **Material and methods:** We conducted cross sectional record-based study of patients diagnosed and treated for genitourinary tuberculosis in the Department of Urology, IGMC Shimla from January 2017 to November 2020.

Results: Eighty-six patients were treated for GUTB and mean age of patients was 42.2 years (18-78 years). In clinical presentation, irritative voiding symptoms i.e., frequency and dysuria (80.23% and 46.51% respectively) were the most common, followed by flank pain and weight loss (40.69% each), further followed by low grade fever (34.88%) and hematuria (33.72%). All patients were started on ATT from DOTS center and then were transferred to local DOTS units of their respective districts. Three patients required modification of ATT due to significant side effects. One patient died as a result of complications related to ATT and comorbid illness. Ultrasound guided percutaneous nephrostomy (PCN), Double J stenting and pigtail drainage for psoas abscess was done in 24 (27.91%) patients, 22 (25.58%) patients and in 8 (9.3%) patients respectively. Reconstructive surgery was done in 25 patients i.e., ureteroureterostomy in 3 (3.48%) patients, ureteric reimplant in 14 patients (16.27%) patients, augmentation ileocystoplasty in 4 (4.65%) patients, Boari flap in 4 (4.65%) patients. Nephrectomy was done in 3 (3.48%) patients and cystectomy with ileal conduit was done in 3 (3.48%) patients. **Conclusion:** GUTB is a prevalent disease in our country although data regarding GUTB is quite limited. GUTB complaints are mostly trivial and nonspecific but consequences are grave. Proper early diagnosis and timely management can prevent morbidity and potential mortality in these patients. Timely intervention and reconstructive surgery is required in a significant number of patients to preserve kidney, ureter, and urinary bladder function.

Keywords: GUTB: Genitourinary tuberculosis, NAATs: Nucleic Acid Amplification Tests, DJ Stenting: Double J Stenting, PCN: Percutaneous Nephrostomy

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Introduction

About 10 million people got infected with tuberculosis (TB) in 2019 worldwide. Out of 10 million 5.6 million were men, 3.2 million women and 1.2 million children. Almost 1.4 million people died from TB in 2019. It is one of the top 10 causes of death and the leading cause from a single infectious agent (above HIV/AIDS) worldwide. Eight countries account for two thirds of the total, with India leading the count, followed by Indonesia, China, the Philippines, Pakistan, Nigeria, Bangladesh and South Africa [1].

Genitourinary system is second commonest system involved with tuberculosis in developing countries, whereas it is third most common in developed countries. It accounts for 20-40% of all cases of extra pulmonary tuberculosis (EPTB) cases [2].

GUTB most commonly involves kidney (74% cases) followed by epididymis, testis, bladder, ureter and prostate gland. Isolated genital organ involvement is reported in 5-30% of tuberculosis cases [3, 4].

Prognosis of TB is determined by the degree of systemic illness. Younger age, absence of comorbid conditions, compliance to

medications and follow up and good social support system are determining factors for favourable outcome. Whereas older age, low socioeconomic strata with comorbid immunocompromising conditions, delayed presentation of disease are poor prognostic factors in terms of treatment outcome.

Most patients of genitourinary TB can be successfully treated with the standard short-course regimen of 6 months of first-line antitubercular drugs [5].

GUTB is one of most commonly infectious disease encountered by a urologist. Diagnosis of GUTB is often delayed owing to the nonspecific nature of its presentation and most patients present with complications i.e., non-functioning kidney, ureteral stricture, hydro-nephrosis, pyonephrosis, small capacity urinary bladder, infertility etc.

Data regarding GUTB is limited in our country despite of significant patient burden. We intend to describe GUTB patients' burden in Himachal Pradesh, their presentation, diagnosis and treatment, especially surgical perspective.

Materials and methods

In this cross-sectional record-based study, patients with diagnosis of GUTB, who were treated in urology department of IGMC Shimla from January 2017 to November 2020, were included in the study. The study was approved by institute ethics committee and conducted as per protocol. The case record forms of the patients diagnosed with

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GUTB were retrieved and analyzed for clinical presentation, urine routine examination, urine for AFB smear test, NAATs for tuberculosis, urine culture and pus culture. Radiological investigations of GUTB patients i.e., ultrasound, IVP and CT scan reports were also analyzed. Patient's ATT drug intake data was noted. Patient's operative details i.e., cystoscopy, DJ stenting, PCN, pigtail drainage of pus, and details of urological surgery if any pertaining to GUTB were retrieved. The analysis of data of symptoms, diagnostic investigations (micro-biological, radiological) and urological procedures pertaining to GUTB was done by epi info software.

Observations

Eighty-six patients were treated for GUTB and mean age of patients was 42.2 years (18-78 years). There were 42 females and 44 males in our study. Ten patients had comorbid conditions like DM, COPD, HTN. Seventy-nine patients were married and seven patients were unmarried. Past history of tuberculosis was present in 6 patients. In clinical presentation, irritative voiding symptoms i.e., frequency and dysuria (80.23% and 46.51% respectively) were the most common, followed by flank pain and weight loss (40.69% each), further followed by low grade fever (34.88%) and hematuria (33.72%) (Table 1).

Table 1 :Clinical and diagnostic parameters across the study population

Parameters	Patients with GUTB (n=86)
Age (years), mean	42.2 years
Male	44 (51.16%)
Female	42(58.83%)
Clinical parameters	
Frequency of urination	69 (80.23%)
Dysuria	40 (46.51%)
Flank pain	35 (40.69%)
Weight loss	35 (40.69%)
Fever	30 (34.88%)
Hematuria	29 (33.72%)
Microbiological /histopathological parameters	
Urine for AFB positive (Z N-staining)	54 (62.79%)
NAATs	
PCR	5
Xpert/CBNAAT	18
	23 (26.74%)
FNAC	2 (2.32%)
Histopathology	10 (11.62%)

Urine microscopic examination revealed pyuria in 78% patients, microscopic hematuria in 65% and routine culture sensitivity was positive in 25 % patients. GUTB was diagnosed in 54(62.79%) patients on the basis of urine AFB positivity on Ziehl- Neelsen staining. NAATs established the diagnosis of GUTB in 23 (26.74%) of patients in our study. FNAC and histopathology established the diagnosis of GUTB in 2.32% and 11.63% of patients respectively. Ultrasonography revealed dilatation of pelvicalyceal system in 37(43%) patients, psoas abscess in 5 (5.8%) patients, renal

abscess in 2(2.32%) patients and perinephric abscess in 1(1.16%) patient. Intravenous urography/ CT urography was done in 58 (67.44%) patients and it revealed kidney to be the primary site of involvement in 59.30% patients (Table 2). Calcification/ thickened walls of ureter and bladder were apparent in 28 (32.55%) patients , lower ureteric or VUJ stricture was noted in 16 (18.6%) patients, whereas 3 (3.5%) patients had multiple ureteral stricture and small contracted urinary bladder was observed in 6 (6.9%) patients (Fig. 1 and 2).

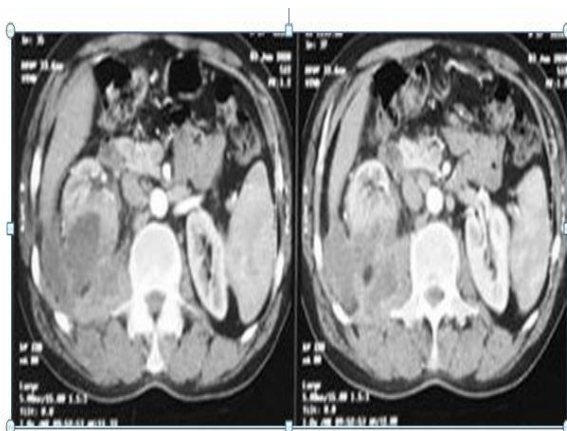


Fig 1:CT Scan showing renal abscess and perinephric abscess



Fig 2:a)CT axial film showing calcification in left kidney, b)CT Urology showing right lead pipe ureter c)Upper ureteric and lower ureteric structures

Table 2 :Radiological findings in GUTB patients

USG findings		Radiological Finding	No. of Patients
			Dilatation of PCS
	Psoas abscess	5	
	Renal abscess	2	
	Perinephric abscess	1	
	Epididymal abscess	1	
IVU / CT urography	Renal Involvement 51 pts (59.30%)	Calyceal destruction	8
		Infundibular stenosis	2
		PCS dilatation	37
		Nonfunctional Kidney	4
	Ureteral Involvement 47 pts (54.65%)	Calcification/ thickened walls of ureter / U bladder	28
		lower ureteric / VUJ stricture	16
		Multiple ureteral stricture	3
U Bladder Involvement 6 pts (6.97%)	Small contracted U bladder	6	

Diagnosis of prostatic tuberculosis was established in one patient on TRUS guided prostatic biopsy. One patient presented with vesico-vaginal fistula (VVF) and another with infertility. The patient with infertility had beaded vas and diagnosis of GUTB was made on aspiration and FNAC of epididymal swelling. Double J stenting was done in 22 (25.58%) patients as a part of internal diversion procedure. USG guided PCN was done in 24 (27.91%) patients i.e., in patients having echogenic content in dilated PCS or in whom DJ stenting was not possible. Three patients required DJ stenting as well as USG guided PCN. Pigtail drainage of abscess under USG guidance was required in 8 (9.3%) patients. All patients were initiated on ATT from DOTS center and were later transferred to

local DOTS units of their respective districts. Three patients required modification of ATT due to significant side effects. One patient died as a result of complications related to ATT and comorbid illness. Patients were followed up with urine for AFB examination and radiological investigations. Definitive ablative/ reconstructive surgical procedure if required was planned later, after assessing the functional status of kidney and structural defect in genitourinary system. Urethroscopic examination of all of the patients was done to assess the extent of disease. DTPA/ EC renal scan was done in 52(60.46%) patients to assess the kidney function, prior to reconstructive surgery of upper urinary tract and to monitor the effect of therapy.

Table 3: Surgical procedures

Operative procedures		No. of patients
Minimal Invasive procedures	Double J Stenting	22(25.58%)
	Ultrasound guided PCN	24(27.91%)
	Pigtail drainage	13(15.12%)
Ablative/Reconstructive surgical procedures	Ureteric reimplantation	14(16.27%)
	Ureterouterostomy	3(3.48%)
	Augmentation ileocystoplasty	4(4.65%)
	Boari flap	4(4.65%)
	Nephrectomy	3(3.48%)
	Cystectomy with ileal conduit	3(3.48%)

Ablative/Reconstructive surgical procedure was required in 31 (36.04%) patients (Table 3). Ablative surgical intervention i.e. nephrectomy was done in three patients for nonfunctional kidney with persistent symptoms and other three patients underwent cystectomy with ileal conduit diversion. Reconstructive surgery for ureteral stricture i.e., ureteric reimplantation and ureterouterostomy was done in 14 patients and 3 patients respectively, whereas Boari flap interposition for long segment ureteral defect was performed on 4 patients. Augmentation ileocystoplasty was done in 4 patients with contracted urinary bladder after the infection was brought under control.

Discussion

The term 'genitourinary tuberculosis' was first used by Hans Wildbolz in 1937. GUTB is usually seen as delayed manifestation of prior symptomatic or asymptomatic pulmonary tubercular infection. Metastatic spread of organism through blood stream during the initial infection leads to tuberculosis of genitourinary system. Reactivation of these dormant bacilli owing to failure of immune system leads to active GUTB with reported latency period ranging from 5-40 years [6]. GUTB, which accounts for 20-40% of extrapulmonary tuberculosis (EPTB) cases, is the second most common site in developing and third most common site of TB in developed nations.

In India, the incidence of GUTB is 18% [6]. GUTB affects men more than women (2:1), seldom children, with a mean age of 40.7 (range 5-90). In our study, patients' age ranged from 18-78 years with mean age of 42 years, with 42 females and 44 males. Different studies have reported varied sex variability [7, 8]. GUTB most commonly affects the kidney accounting for 74% of cases. Chronic latent pulmonary infection spreads to the kidneys, epididymis, or fallopian tubes through hematogenous route; prostate seeding has also been reported but is rare. Other genitourinary organs are involved by local invasion [5]. In our series renal involvement was seen in 51 (59.30%) patients and out of these 4 (4.65%) patients had nonfunctional kidney. Our 6 (6.9%) patients of GUTB had past history of pulmonary tuberculosis. Krishnamoorthy et al and Singh et al, in their studies reported history of pulmonary tuberculosis in GUTB patients in 22.7% and 19.66% of cases respectively [7, 8]. In our series pelvicalyceal dilatation was seen in 37(43%) patients whereas two (2.32%) patients had infundibular stenosis owing to fibrous tissue causing stricture in calyceal stem. Tubercular ureteritis is usually an extension of renal disease and the most commonly affected site is uretero-vesical junction. Fibrosis of ureter may occur during treatment leading to scarring and stricturing of ureter and resultant hydronephrosis. Urinary bladder lesions are secondary to renal tuberculosis and the

initial forms of infection affect the mucosa around ureteric orifice. As disease progresses, inflammation involves muscle. The fibrosis starts around ureteral orifice resulting either in stricture formation with HDN or become withdrawn and dilated (i.e., golf-hole appearance) with vesicoureteral reflux. In advanced cases deep muscles of entire bladder wall are replaced by fibrous tissue resulting in non-functional, small contracted irregular urinary bladder. In study by Ahsan A et al. kidney was most commonly affected genitourinary organ (62.26%). They observed involvement of ureter in 30.19%, U bladder in 24.53%, prostate in 9.43% and epididymis in 1.89% of their patients. 16 out of their 53 GUTB patients had ureteral stricture with lower ureter being involved in 14 cases. 11 of their patients had U bladder involvement, out of which 6 had small capacity contracted urinary bladder [9]. Bansal P et al reported renal involvement in 34 out of 60 GUTB patients. U bladder was involved in 25 patients, ureteral lesions were found in 20 patients, epididymal involvement in 2 patients whereas, complex lesion (more than two sites involvement) was reported in 6 patients [10]. In our study, kidney was the most common site of involvement i.e., in 59.30% of cases. Calcification/thickened walls of ureter and bladder were apparent in 28 (32.55%) patients, lower ureteric or VUJ stricture was noted in 16 (18.6%) patients, whereas 3 (3.5%) patients had multiple ureteral strictures and small contracted urinary bladder was observed in 6 (6.9%) patients. We observed prostatic and epididymal involvement in one patient each. The present study showed irritative voiding symptoms (frequency and dysuria in 80.23% and 46.51% respectively) to be the most common symptoms in GUTB patients, followed by flank pain and weight loss (40.69% each), low grade fever (34.88%) and hematuria (33.72%). Patients of GUTB may also present with scrotal mass, perianal sinus, haematospermia, genital ulcer etc. One of the patients of GUTB in our study presented with VVF. Ahsan A et al reported irritative voiding symptoms in 37 (69.81%) and hematuria in 30 (56.60%), recurrent urinary infection in 8 (15.09%) and renal failure in 6 (11.32%) patients with GUTB [9]. In study by Singh JP et al, irritative voiding symptoms (66.47%) were the most common presentation followed by hematuria (47.60%) [8]. Reasons for delayed diagnosis of GUTB are its nonspecific symptoms, gradual progression and latency of the disease, coexistent urinary tract infection and lack of suspicion by the treating physician. Acid fast staining is a cheap and fast method but lacks sensitivity. PCR has been extensively studied and can yield results early with reported sensitivity ranging from 87% - 100% and specificity from 92% - 99.8% in literature. Xpert MTB/ CBNAAT, simultaneously detect mycobacterium tuberculosis complex and resistance to rifampicin within two hours. Altez Fernandez C et al reported its sensitivity ranging from 83% - 95% and specificity from 79% - 99%. [11, 12]. In our study pyuria and positive routine culture sensitivity was noted in 78% and 25% of patients respectively. GUTB was diagnosed in 54 (62.79%) patients on the basis of urine AFB positivity on Ziehl-Neelsen staining. NAATs established the diagnosis of GUTB in 23 (26.74%) of patients in our study. FNAC and histopathology established the diagnosis of GUTB in 2.32% and 11.63% of patients respectively. Kulchavenya E et al reported comorbid UTI in 65.1% of GUTB cases [13]. Singh et al in their study reported 41.60% of positivity rate for urine AFB test, 55.4% for urine M. tuberculosis culture test and 67.7% for PCR [8].

Imaging studies: USG, IVU, CT scan are useful adjuncts in diagnosis of GUTB. IVU provides anatomic details, functional derangement of kidney, ureter, U bladder and helps in defining the extent and severity of the disease [14]. CT scan helps in assessing the extent of GUTB, provides indirect functional status of kidney and is very sensitive for detecting calcification and thickened wall of ureter/ U bladder, apart from its ability to assess other intra-abdominal organs. In the present study PCS dilatation was seen in 43% and calcification/ thickened wall of ureter and U bladder was noted in 32.55% of GUTB patients. GUTB patients carry a lower bacillary load than pulmonary tuberculosis, hence respond better to

short course of ATT, but effective ATT drugs alone may not resolve GUTB. Study by Gupta NP et al emphasized that surgical management is complimentary to anti tubercular drug treatment. In their study, 241 patients underwent surgical procedure (endoscopic 33, ablative 37 and 128 reconstructive procedures) as adjunct to antitubercular drug therapy [15]. In our study, Double J stenting and USG guided PCN was done in 25.58% and 27.91% of GUTB patients as a part of diversion procedure. Three patients required DJ stenting as well as USG guided PCN. Ablative surgical intervention was required in 6 patients of GUTB (nephrectomy in 3 and cystectomy with ileal conduit in 3 patients). Definitive reconstructive surgical intervention was done in 25 patients on completion of 4-6 weeks of intensive ATT drug therapy, after assessing the functional status of kidney and structural defect in genitourinary system. Narrow lumen of ureteral tract is anatomically vulnerable to obstruction, especially in patients who present late and also in due course of ATT drug therapy [15].

Hence, early endoscopic/minimally invasive intervention in desired cases is crucial to preserve renal parenchymal and ureteral function at maximum. However, if ablative or reconstructive surgery is required, it should be planned as elective procedure i.e., after 4-6 weeks of intensive ATT drug therapy to stabilize the active disease.

Conclusion

GUTB is a prevalent disease in our country, although data regarding GUTB is very limited. High index of suspicion and wide range of investigations should be incorporated to achieve early diagnosis. We emphasize that minimally invasive intervention and reconstructive surgical procedure is required in addition to ATT drug therapy in significant proportion of GUTB patients in order to preserve kidney, ureter and U bladder function at maximum.

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