

Aspects of Evolving Genito Urinary Tuberculosis-A Profile of Genito Urinary Tuberculosis (GUTB) in 110 Patients

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ABSTRACT

Introduction: Genito Urinary Tuberculosis (GUTB) is a widespread disease seen in urology practice. The true incidence and prevalence of GUTB is difficult to estimate because a large number of patients remain asymptomatic.

Aim: To recognize typical and atypical clinical and radiological features of tuberculosis and to emphasize the need for diagnosing GUTB early.

Materials and Methods: This was a retrospective study conducted in 110 cases of GUTB diagnosed and treated in two teaching institutions over a period of three years, from July 2002 to June 2005. A detailed history, thorough clinical examination, urine examination, culture for tubercle bacillus, imaging studies, cystoscopy and histological and serological examination were done to arrive at a diagnosis.

Results: Fifty six patients (51%) were in the age group of 21-40

years. The male: female ratio was 1.4: 1. Loin pain was the most common symptom observed in 27% of the patients. Intravenous Urogram (IVU) revealed non-visualised kidney in 25 patients (23%), hydronephrosis or hydrouretero nephrosis in 34 patients (31%) and distortion, cavitation or scarring of the calyces in 16 patients (14.5%). Five of them had thimble bladder. In 14 patients, IVU appeared normal. About 28 patients (25%) were treated conservatively with anti tuberculosis therapy. Twenty one of them (19%) underwent Nephrectomy and 10 patients had reconstructive procedures.

Conclusion: A peculiarity of most of our patients was a late presentation with advanced disease. Most patients were asymptomatic or ignorant. Slow but continuous infection causes a destruction of renal parenchyma and the healing process leads to renal parenchymal loss. If identified early and treated appropriately, GUTB is a curable condition.

Keywords: Acid fast bacilli, Hydronephrosis, Nephrectomy, Tubercle bacillus, Tuberculoma

INTRODUCTION

GUTB is one of the common urological causes for infection related morbidity [1]. The term GUTB was coined by Wildbolz, who stressed that renal tuberculosis and epididymal tuberculosis were not diseases of isolated organs, but different examples of the same disease carried by the bloodstream [2]. The true incidence and prevalence of GUTB is difficult to estimate because a large number of patients remain asymptomatic and the disease is not looked for in these asymptomatic patients. Moreover, the urine can become sterilized relatively rapidly after the initiation of chemotherapy, further adding on to the diagnostic difficulties.

Tuberculosis (TB) continues to be a major health problem in India. Nearly one third of the global TB burden is contributed by India alone [3]. After lymphatic involvement, GUTB is considered the most common manifestation of extra pulmonary tuberculosis worldwide [4]. Renal tuberculosis is the most common site of extra – pulmonary GUTB comprising of 20% of all extra pulmonary tuberculosis [5]. It usually results from silent bacillemia accompanying pulmonary Tuberculosis. However, active lesion in the kidney may not become clinically apparent for many years. Also, many cases remain clinically dormant for even years together. This infection can result in caseation and destruction of the renal parenchyma and healing leads to strictures, obstruction and infection causing renal functional loss and failure [6].

Primary care physicians provide the critical first steps in reducing the incidence of active cases and detecting the true emergence of drug resistance in TB [7]. Lack of a definite standardized treatment regime for various forms of urogenital tuberculosis by Revised National Tuberculosis Control Program, over-diagnosis of GUTB

based on presumptive diagnosis by primary care physicians and urologists, emerging resistant strains in ever-increasing Human Immuno deficiency Virus victims in our country have further complicated the already existing difficulties in treating these patients effectively and efficiently [8,9].

The main objectives of this study are to recognize typical and atypical clinical and radiological features of tuberculosis, to motivate the physician to make a diagnosis more frequently and also to lay emphasis on the need for standardization of treatment regimen.

MATERIALS AND METHODS

This was a retrospective study in 110 patients of GUTB diagnosed and treated in two teaching institutions in Chennai, Tamil Nadu, India over a period of three years from June 2002 to May 2005. Care has been taken to avoid disclosure of patients' identity in any form. As this study was a retrospective one, informed consent from the patients and Ethical Committee clearance was not obtained.

The criteria for diagnosing GUTB in these patients were classified into two groups. The first group of 74 patients (67%) included those with proven Tuberculosis, as determined by urine for Acid Fast Bacilli (AFB) smear, AFB culture, histopathological evidence of Tuberculosis and/or by serological methods. The second group of 36 patients (33%) included those with presumed tuberculosis who had two or more of the following features on urological imaging or endoscopic evaluation in the absence of demonstration of acid fast bacilli either in urine smear or in culture or in histopathological examination: small capacity or thimble urinary bladder, golf-hole ureteric orifices, thickened or beaded epididymis, ureteric strictures, renal infundibular narrowing with focal caliectasis or renal calcifications. This classification into two

groups was done only for the description of cases and not with intent to include patients for any form of statistical analysis.

All patients were assessed with a detailed history, a thorough clinical examination, serum biochemistry, urine culture, Chest X-Ray and Ultra sonogram. Early morning specimen of urine was also examined for Mycobacterium on three consecutive days and Intravenous Urography was done in all these patients.

Cystoscopy and bladder mucosal biopsy were performed in patients in whom the diagnosis was in doubt or during an interventional procedure (JJ stenting or Retrograde Ureteropyeloscopy). Serological testing for 16KDa, 27KDa and 38KDa antigens was done in those selected group of patients, who had a strong clinical suspicion of tuberculosis in whom all these investigations were normal.

RESULTS

Fifty six patients (51%) in our study were in the age group of 21-40 years and 43 patients (39%) were between 41-60 years of age. The minimum age was 11 years and maximum was 67 years, with the average age being 35.4 years. There were 65 males and 45 females with the male-female ratio being 1.4:1. The various modes of presentation are listed in [Table/Fig-1]. Loin pain was the most common presentation, seen in 30 patients (27%) followed by lower urinary tract symptoms in 28 patients (25.5%). One patient with HIV presented with features of sub acute intestinal obstruction before a diagnosis of gastro intestinal and genito urinary tuberculosis was made.

Three patients (2.7%) had gastro intestinal tuberculosis and one patient had been treated for retrobulbar tuberculoma. Twenty five patients (22.7%) had associated pulmonary tuberculosis treated in the past. [Table/Fig-2] shows the time interval between the onset of primary pulmonary tuberculosis and development of urogenital tuberculosis. More than 50% of them (n=13) had a mean interval of 3-10 years.

[Table/Fig-3] shows the various diagnostic modalities employed in our study. In those patients who had a strong clinical suspicion of GUTB, and in whom all the investigation modalities were normal, serological diagnosis using 16 KDa, 27 KDa and 38 KDa antigens were made. Six out of 36 patients were tested positive for tuberculosis by this method.

A total of 80 patients needed some form of surgical intervention or the other. Of these, 57 were from Group 1 and 23 were from Group 2. [Table/Fig-4] describes the list of various surgical procedures done. Minimally invasive procedures required were Percutaneous nephrostomy and internal DJ stenting were done in 13 and 26 patients respectively as a part of initial diversion procedures. These patients were followed up with anti tuberculous therapy and a definitive therapy was planned later after assessing the functional status of the kidneys. Twenty one patients ended up with nephrectomy. Four of them needed nephroureterectomy. In those patients with renal involvement (n=70), eight of them had associated ureteric involvement and four had associated bladder involvement (n=12). Renal involvement was the most commonly observed finding in our study (n=70). [Table/Fig-5] describes the radiological findings of a 40-year-old lady with right hydronephrosis and a poorly functioning right kidney. Such patients performed well after nephrectomy.

Ureteric involvement was the second most common finding observed in our study (n=30). While a majority of them (n=20) settled with minimally invasive procedures like Double J stenting or a percutaneous nephrostomy, 10 patients needed reconstructive procedures in the form of boari flap or ureteric reimplantation. Six patients needed only a simple ureteric reimplantation but four of them with a long segment defect of the ureter needed Boari flap. [Table/Fig-6] describes the steps of classical Boari flap reconstruction.

Six of the patients with bladder involvement (n=18) had a severely contracted (thimble) bladder that needed an augmentation. [Table/

Fig-7] describes the radiological findings of a thimble bladder and the steps of augmentation cystoplasty.

Eighteen patients underwent reconstructive procedures. Boari flap was performed in four patients, Augmentation cystoplasty in six patients, Uretero calycostomy in two patients and Ureteric reimplantation in six patients. Corticosteroids were not used as a routine in our study, but were needed for four patients. These included two patients with tuberculous meningitis and one patient with retro bulbar tuberculoma. The fourth patient had Ethambutol induced retro bulbar neuritis and was started on corticosteroids. None of them had received corticosteroids for urinary tuberculosis.

Genital tuberculosis was not uncommon. Six patients had involvement of epididymis. One patient had primary tuberculosis of the glans penis mimicking malignancy. His wife was on treatment for pulmonary tuberculosis. On initiation of Anti Tuberculous Therapy (ATT), the lesion melted and eventually disappeared [Table/Fig-8].

All patients were followed up with serial ultrasound KUB region at the end of intensive phase of anti tuberculous therapy. A 20 minutes single shot IVU film was taken at the end of intensive phase of chemotherapy.

Urine for AFB smear and culture were done in those patients who had been tested positive initially. Five patients lost to follow up during the course of their treatment and three patients expired while they were on treatment with ATT.

Features	No.	%
Loin pain	30	27.3
Storage symptoms	28	25.5
Haematuria	12	11.0
Stone disease	10	9.1
Palpable mass	9	8.2
Scrotal sinus	6	5.5
Infertility	3	2.7
GI symptoms	3	2.7
Urosepsis	2	1.8
Renal failure	2	1.8
Neck sinus	1	0.9
Calcified kidney	1	0.9
Urinoma	1	0.9
Recurrence	1	0.9
PUO	1	0.9
TOTAL	110	100

[Table/Fig-1]: Various modes of presentation of GUTB in our study.

Duration	Number
Concurrent	4
Less than one year	2
1- 3 years	2
3-10 years	13
More than 10 years	4

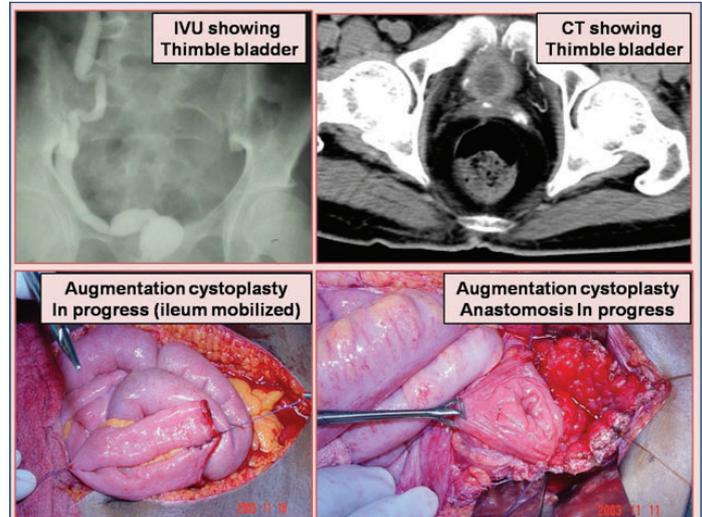
[Table/Fig-2]: Time interval between primary pulmonary tuberculosis and onset of GUTB.

Diagnostic modality	No.	%
Urine AFB smear	23	21
Urine AFB culture	6	5
Cystoscopy –bladder biopsy	19	17
Histopathology of resected specimen	14	13
Serology	6	5
Scrotal sinus biopsy	6	5
Presumed diagnosis including radiological diagnosis	36	33

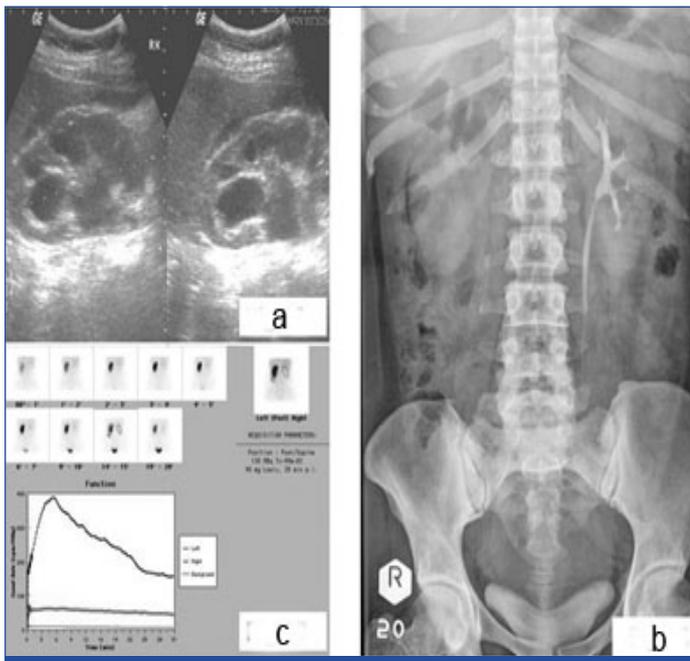
[Table/Fig-3]: Various diagnostic modalities employed in our study.

Organ involved	No.	Procedure performed	No. of patients	% who underwent procedure
Kidney (Open procedures)		Nephrectomy	21	30
		Nephroureterectomy	4	5.7
		Ureterocalycostomy	2	2.9
		Total number of open procedures	27	38.6
Kidney (Minimally invasive procedures)	70	Percutaneous nephrostomy	13	18.6
		DJ stenting	26	37.1
		Both PCN and JJ stenting	7	10
		Total minimally invasive procedures	32 (39-7)	(55.7 - 10)
Ureters	30	Boari flap	4	13.3
		Ureteric Reimplantation	6	20
Bladder	18	Augmentation cystoplasty	6	33.3
Prostate (incidental)	4	Trans urethral resection of prostate	4	100
Penis	1	--	--	--
Testis and Epididymis	6	Low orchidectomy	1	17
Total 117 (129 - 12)	Total		80	68.4

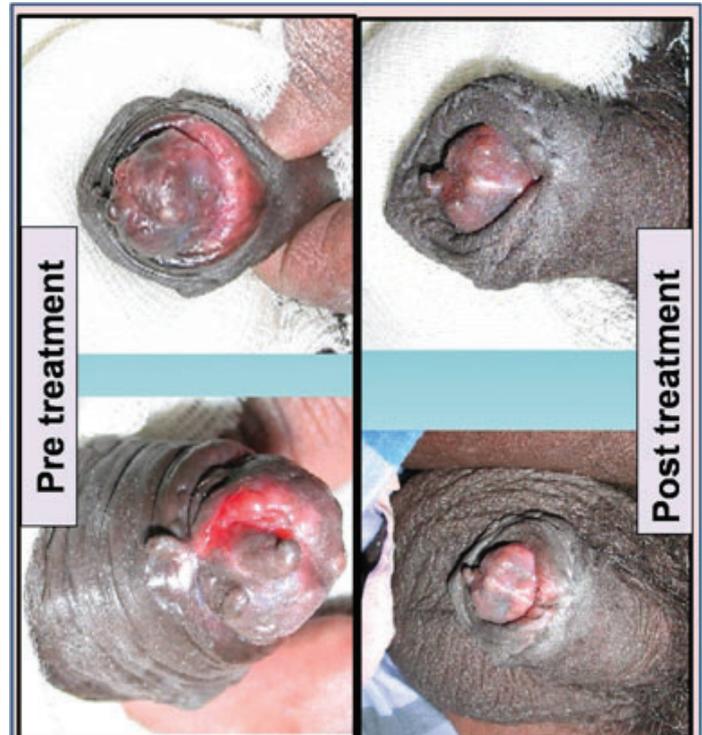
[Table/Fig-4]: Details of the organs involved and surgical procedure performed in GUTB patients.



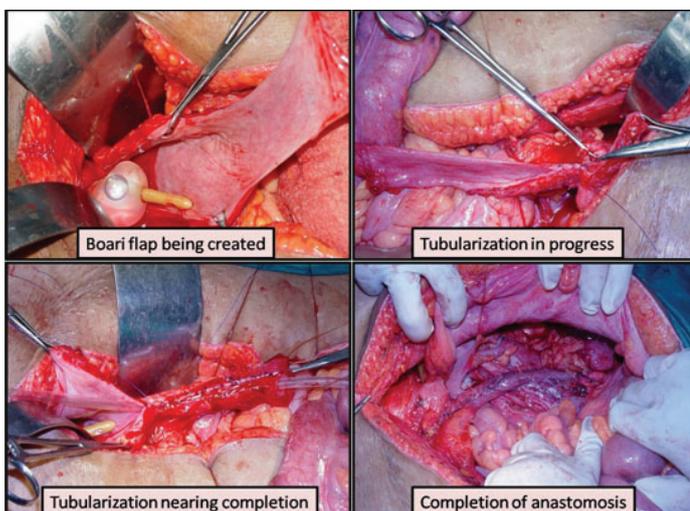
[Table/Fig-7]: Augmentation cystoplasty in progress.



[Table/Fig-5]: Radiological findings of a poorly functioning right kidney.



[Table/Fig-8]: Pre and post treatment images of TB penis.



[Table/Fig-6]: Classical Boari flap reconstruction in progress.

DISCUSSION

Renal Tuberculosis is the most common form of extra pulmonary tuberculosis. From the time, the term GUTB was first coined by Wildbolz, various studies have shown that up to 15% of patients with pulmonary tuberculosis are expected to develop GUTB over time [10]. The incidence of GUTB has markedly decreased in the west but the situation has not altered much in developing countries [11]. Eight million new cases of tuberculosis occur each year and three million patients die of tuberculosis every year [12]. Silent haematogenous spread from the primary infection seeds the cortices of both the kidneys and can remain dormant for decades with potential for reactivation at a later date [13,14]. Most of our patients presented in an advanced stage making salvageable procedures even more difficult [15-17].

Of the 110 of our patients, 65 were males and 45 were females. The male preponderance has been reported in various other studies also [18]. The age group ranged from 11 years to 67 years, with a mean age of 35.4 years. GUTB usually presents in adults because of the time lapse between primary infection and renal tuberculosis, with a mean interval of 3-10 years. However, it can also present in childhood as in one of our patients, who was just 11-year-old. Miliary

tuberculosis can also cause concurrent renal disease in children. Involvement of the kidneys is the most common form of tuberculous involvement of the genito urinary tract. The most frequent clinical features reported in literature have been frequency, dysuria, loin pain and haematuria. Amaresan MS et al., reported loin pain in 33% and dysuria in 42% of his patients [19]. In our study, 27% had loin pain and 26% had voiding symptoms.

Traditionally, GUTB is diagnosed by the demonstration of tubercle bacilli in urine or by the presence of acid fast bacilli in the histopathology specimen. In those specimens where demonstration of the bacillus in the biopsy specimen is not possible, many a time, indirect evidences like presence of epithelioid granulomas and Langhans giant cells are considered adequate enough to start the patients on ATT. Urine smear for AFB is a simple screening test which can clinch the diagnosis. The major limitation is that there can be confusion in distinguishing *Mycobacterium smegmatis* from the tubercle bacillus. Moreover, in view of intermittent bacilluria, three to five consecutive days urine examination is required to document the infection. The yield of direct AFB smear is very low and is only 30% [20]. Moreover, culture medium for tuberculosis also takes a longer time upto six to eight weeks. The specificity is considerably higher than with urine smear for AFB [21]. Polymerase Chain Reaction (PCR) for tuberculosis can detect the AFB within a few hours of DNA extraction. This will be positive even if the smear and culture tests are negative. But the main pitfall is that non tuberculous mycobacteria or haemoglobin in haematuria can lead to false PCR negativity [22]. Collection of multiple samples of urine, removal of inhibitors of PCR, centrifugation of urine before the analysis, to a large extent might decrease the incidence of false negativity [23].

Primary tuberculosis of penis is very rare. Earlier it was seen as a complication of ritual circumcision, when it was the practice of the operators to suck the penis [24]. It also occurs after coital contact with organisms already present in the female genital tract or by contamination from infected clothing [25]. Secondary penile tuberculosis occurs as a secondary manifestation of active pulmonary tuberculosis.

The differential diagnosis of GUTB requires identification of mycobacterium in urine smear or by culture methods. In western countries, 90% of the affected patients had a positive culture [26]. In our study, urine smear for mycobacteria was positive in 21% and culture positive in 5% of the patients. More over 33% of the patients were treated based on presumed diagnosis [Table/Fig-9].

In spite of better imaging modalities available that can identify the disease at a much earlier stage, and with the availability of effective antitubercular drugs, surgery still holds the centre stage in the management of GUTB [27]. Gupta NP et al., in one of the largest series of GUTB cases, in 2006, stated that surgical management is complementary to antitubercular chemotherapy. They proposed a waiting period of four to eight weeks of ATT before any surgical intervention is planned. According to their study, this waiting period allows the lesion to stabilize well and also helps in better planning of the proposed reconstructive procedure surgery [28].

The problems that we faced in management of these patients were that most of these patients presented in an advanced stage, in whom inspite of an initial attempt to salvage the kidney by way of percutaneous nephrostomy or JJ stenting in 39 (35%) of our patients, 21 (19%) of them ended up in nephrectomy.

Treatment	Our study (%)	Ramanathan R et al., (%) [15]	Najar MS et al., (%) [5]
On confirmation of diagnosis	67	70	54
Presumptive diagnosis and empirical treatment	33	30	46

[Table/Fig-9]: Comparison with other studies regarding indication for treatment with ATT.

Fleschner and Gow reviewed 300 cases of GUTB of which 69 patients (23%) with non-functioning kidney underwent Nephrectomy [29]. Late presentation and advanced disease at the time of presentation could be an explanation for this high incidence of nephrectomies [30]. Poor patient compliance and inability to adopt DOTS to the fullest extent were the other problems that we faced in our study. However, Jitendra Singh, in his study on 117 cases of GUTB had adopted short course chemotherapy with standard Category I regime and achieved an Eighty six percent response to anti tubercular therapy [23].

Tuberculosis occurs in the seminal vesicle in males and in the uterus and fallopian tube in females through the haematogenous or lymphatic route [31]. In our study, we did not encounter any patient having seminal vesicle or uterine involvement.

LIMITATION

The major limitation of our study was that ours was a retrospective study. The other issues that we faced in making a diagnosis of GUTB were that, only about one fourth (26%) of the patients were either smear or culture positive. More over one third (33%) of the patients were treated based on presumed diagnosis. Lacks of facility to diagnose atypical mycobacteriae, antibacterial sensitivity or multi-drug resistant strains were the other limitations. However, to the best of our knowledge, by a thorough pubmed search from 1960 onwards till date, this study has been the third largest series to be ever reported in published literature after Wechsler H et al., and Singh JP et al., who reported 127 and 117 cases of GUTB respectively [32,33].

CONCLUSION

As urinary tuberculosis is a great mimicker, a high index of suspicion is necessary to make a diagnosis of GUTB. Diagnosis based on clinical findings alone may lead to over treatment. In view of intermittent bacilluria one is justified in initiating treatment based on clinical and radiological findings of TB. Delay in presentation and diagnosis leads to severe sequelae resulting in a non-salvageable state. Since atypical mycobacteria are resistant to many of the first line drugs, the principles of therapy for atypical mycobacteria may require attention.

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