



Research Article

CLINICAL SPECTRUM AND MANAGEMENT OF GENITO-URINARY TUBERCULOSIS IN A TERTIARY CARE CENTRE-INSTITUTIONAL EXPERIENCE -A PROSPECTIVE STUDY

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ABSTRACT

Background: Tuberculosis had been declared by the World Health Organization (WHO) as ‘public health emergency’ in 1993. Extra pulmonary tuberculosis (E.P.T.B.) comprises 20-25% total burden of the disease in which genitourinary tuberculosis (G.U.T.B.) is 4%. Timely diagnosis and treatment will prevent the sequelae of this disease.

Aims: To know the varied clinical presentations, diagnostic modalities and management of G.U.T.B.

Material and Methods: The study population comprised 46 patients who were diagnosed with GUTB admitted in our institute from August 2016 to March 2018. They were analysed for clinical presentation, diagnostic modalities and management.

Results: Young patients mainly in third decade of life were commonly affected with higher incidence in females. In our study, the most common presentation was irritative voiding symptoms (73.91%) followed by Flank pain (39.13%). Although it can affect the entire organ in genito-urinary system but, in the present study, kidney was the most affected organ (73.91%) following ureter (30.43%), urinary bladder (17.39%), prostate (2.17%) and epididymis (2.17%)... In this study, we had not encountered any case of testicular and penile tuberculosis. Among the different diagnostic modalities in this study, the diagnostic positivity rate was 41.6% for the urine AFB test, 55.4% for the urine *M. tuberculosis* culture test and 67.7% for PCR. Chest x-ray was positive in 25.6%. ESR was raised in 62.5% patients.

Conclusion: A high index of suspicion and a wide range of investigations may be required to achieve a complete diagnosis of genitourinary tuberculosis. Though short course chemotherapy with four-drug-regimen for six month-duration is the mainstay of treatment, surgical interventions were required in 58.69% of cases of this study.

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INTRODUCTION

Tuberculosis (TB) is one of the leading causes of infectious diseases’ morbidity and mortality¹. Tuberculosis had been declared by the World Health Organization (WHO) as ‘public health emergency’ in 1993^{1, 2}. Extra-pulmonary tuberculosis (E.P.T.B.) comprises 20-25 % total burden of the disease in which genito-urinary tuberculosis (G.U.T.B.) is 4%. In India, the incidence of GUTB is 2.2 million/year (worldwide six million new cases), with a mortality rate of 29/100,000 population/year and prevalence of TB is 168/100,000 population/year.^{1,2} Timely diagnosis and treatment will prevent the sequelae of this disease. The objective of study was to know the varied clinical presentations, diagnostic modalities and management of G.U.T.B. in tertiary care centre.

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MATERIAL AND METHODS

This prospective study of a total of 46 patients with GUTB, who were admitted between August 2016 to March 2018 in the Urology Department of Kilpauk medical college & government Royapettah hospital Chennai. All cases were diagnosed with clinical presentation, urine AFB smear, urine *M.tuberculosis* culture, urine PCR (polymerasechain reaction) for *M. tuberculosis*, radiological and histopathological examinations.

RESULTS

Most patients were in their third decade of life (63.2%) and there was female sex dominance (Table 1). Irritative voiding was the commonest presentation and most of the patients had more than one presenting features. A past history of pulmonary tuberculosis was detected in 4 (8.69%) patients and spine tuberculosis in one.

Urinalysis was non-specific, revealed sterile pyuria in 27 (58.69%), proteinuria in 31(67.39%), and hematuria in 8 (17.39%) patients.

Intra venous pyelogram (I.V.P.) was done in all patients. In I.V.P, kidney was the major primary site of involvement followed by ureter and bladder (Table 2). In all films, no specific type of common deformity was seen.

Table 1 Characteristics GUTB patients in study

Total number of cases		46	
Male to female ratio		1-1.51	
Presentation		Total no. of patients	Percentage%
Irritative voiding symptom		34	73.91%
Hematuria		8	17.39%
Flank pain		18	39.13%
Constitutional symptoms		14	30.43%
Recurrent urinary track symptoms		10	21.73%
Scrotal mass		1	2.32%
Associated with renal failure		8	17.39%

Table 2 Site of involvement in IVP in GUTB patients

Organ involved	Number of patients	Calyx and infundibular deformity	Hydronephrosis	Non-functioning kidney
Kidney	34	15	11	8
Ureter	14	Stricture(lower ureter) 2	Multiple stricture 2	others 10
Bladder	4			

Table 3 Organs involved and surgical procedure performed in GUTB patients

Organ involved	Procedure done	No of Patients underwent procedure	Percentage of patient underwent procedure
Kidney(34)	Nephrectomy	6	17.64%
	Nephroureterectomy	2	5.88%
	D-J Stent Insertion	11	78.57%
Ureter(14)	Nephrostomy placement	3	21.42%
	Ureteric Reimplantation	2	14.28%
	Ileal ureter with caeco cystostasty	1	7.14%
Bladder(8)	Augmentation cystoplasty	4	50%
Prostate (1)	TURP (Incidental)	1	

All patients were scheduled to receive 6-month chemotherapy with isoniazid, rifampicin, and ethambutol or pyrazinamide according to the Centre for Disease Control and American Thoracic Society protocol. As for adverse reactions, abnormal liver function was observed in three, pruritus in two and skin eruption in one. At least one of the urine tests (urine AFB test, urine culture test and PCR) was positive in 32 (69.56%) patients before the start of chemotherapy, but it became negative in all patients within three months of chemotherapy. Surgical procedures were needed in 27 (58.69%) patients. (Table 3).

DISCUSSION

The term GUTB was first introduced by Willbolz *et al.* It is the second most common form of extra pulmonary tuberculosis after lymph node involvement.⁴ Although GUTB was the most common sub-type of extra-pulmonary tuberculosis (EPTB), it was recently reported to account for <5% of all patients with

EPTB.¹⁸ 8 to 15% of patients with pulmonary tuberculosis are supposed to be at risk of developing GUTB.⁵ In our study, 8.69 % of patients had the history of pulmonary tuberculosis.

Active GUTB usually presents 5-25 years after the primary infection⁶. The primary organ affected in urinary tract is kidney. Renal involvement is usually slow, progressive and destructive. It may lead to unilateral renal loss and renal failure in bilateral involvement. Other part of urinary tract is involved as extension of disease from kidney.

In our study, kidney was involved in 73.91 % and 17.39%% had associated renal failure.

In the genitalia, primary site of infection is epididymis in males and fallopian tube in females. Involvement of the genital tract usually occurs in the reproductive age group.⁷ The epididymis are affected in 10 to 55% of men with urogenital tuberculosis.⁷ It may manifest as an acute infection, chronic infection or infertility. Acute infection may manifest as a combined epididymo-orchitis with pain, tenderness and scrotal swelling. This may be the commonest manifestation in up to 40% cases⁷. The other common presentation is a scrotal or testicular mass or abscess with or without pain.⁸ Infertility may be the presenting feature in about 10% cases.

The sperm counts and motility may be reduced due to blockage of the vas and/or secondary atrophy⁹. Epididymal tuberculosis is bilateral in 34% of cases, presenting as a nodule or scrotal hardening in all patients, scrotal fistula in half of cases, and hydrocele in only 5%¹⁰. The testis is a rare site for tuberculous involvement. Testicular involvement usually occurs contiguous to the epididymal involvement.⁷

In our study, one patient had epididymis involveent. In our country, possibility of tubercular involvement of epididymis is often forgotten and it is considered due to non-specific infection or filarial origin. Tuberculosis occurs in the seminal vesicle in males and in the uterus and ovarian tube in females through the haematogenous or lymphatic route.¹⁰

Prostate tuberculosis is rare.¹¹ Route of infection may be either haematogenous or descending. Although such patients are mostly asymptomatic, but a few advanced cases may present as perineal sinus or decrease ejaculatory volume. On digital rectal examination, the gland is usually non-tender, nodular and rarely enlarged. The diagnosis is most often made by pathologists after prostate biopsy or TURP.¹¹⁻¹³ In our study, one patient had prostate T.B.;

In our series, irritative voiding symptoms were seen in 34 (73.91%) cases, flank pain in 18(39.13%) cases, haematuria in 8 (17.39%) cases. 5 (21.73%) had, recurrent urinary infection. The incidence of renal failure in our series was 8 (17.39%). The delayed diagnosis is due to the insidious progression, paucity or non-specificity of symptoms, lack of physicians' awareness and bizarre presentation. Therefore, diagnosis is rarely made before advanced urogenital lesions develop. G.U.T.B. is diagnosed by demonstration of mycobacterium in urine or body fluid and granulomatous lesion on histopathology.

Other features which help in diagnosis are changes in radiographic study (I.V.P, C.T. and Chest X-ray), raised ESR.^{17, 18} Although urine AFB test is simple, economical, and it has low sensitivity and specificity for *M. tuberculosis*. In urine examination, sterile pyuria is a classical finding, but

demonstration of mycobacterium is used as primary test for diagnosis.¹⁷

The yield of direct A.F.B. smear is low and it is positive in 30% of cases.¹⁸

The culture in special medium takes six-eight weeks, but it is sensitive in 20- 97% of cases and has a higher specificity compared with the urine AFB test.^{18, 19} Urine PCR can detect the presence of *M. Tuberculosis* within a few hours of D.N.A extraction from the sample, even when the urine AFB test and the urine *M. tuberculosis* culture test are negative. It has a reported sensitivity approach to 94% with specificity 88%.

In our study, the positivity rate was 41.6% for the urine AFB test, 55.4% for the urine *Tuberculosis* culture test, and 67.7% for PCR. Kimet *al* have demonstrated that non-tuberculous mycobacteria (NTM) or haemoglobin in haematuria can lead to false PCR negativity.^{19, 20} This was the reason of low sensitivity of PCR in our study. Jung *et al* reported that PCR sensitivity in urine was relatively low (60%) and the detection rate of NTM, was also low compared with sputum specimens.^{19, 20}

There are several methods for decreasing false PCR negativity, such as multiple collections of urine samples, collection of high-quality samples such as the first morning urine, removal of inhibitors of PCR, and increasing urine concentration by centrifugation before the analysis.

Imaging tests are important in investigation module of GUTB. Initial tests are plain x-ray abdomen and chest x-ray. Plain X-ray abdomen may show calcification primarily in kidney (7-14%), rarely in ureter, bladder wall or seminal vesicle. USG is poor modality to detect morphological change, but it is more useful in follow up than initial diagnosis.²¹

I.V.U is one of the most useful tests as it provides anatomical as well as functional details of kidney, ureter and bladder. The earliest change detected in GUTB may be loss of sharpness or blunting of minor calyces. With progression, there may be moth-eaten appearance of calyces or lost calyces, infundibular stenosis, renal cavitation, pseudotumour or renal scarring and non-functioning kidney.²² Ureter are initially dilated or irregular and later on with progression, they give beaded or pipe-stem or corkscrew appearance. Healing in TB, with or without chemotherapy, is often accompanied by fibrosis which leads to stricture.



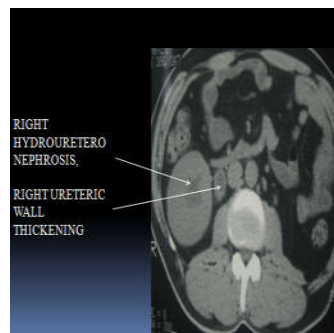
IVU revealing multiple parenchymal cavities with areas of papillary necrosis in the upper group calyces, bilaterally. The (L) upper group (lateral division) calyceal outline is destroyed by adjacent granulomatous tissue

Strictures have been reported in 10-56% of patients with GUTB. Elke *et al* found that ureteric strictures are most

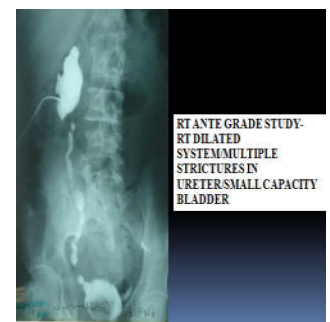
commonly located in distal ureter (56%). Mid ureter was involved in 13% and the proximal ureter in 17.19% has the multiple stricture. Multiple stenosis of the collecting system from the infundibulum to the ureterovesical junction are the findings most suggestive of urogenital tuberculosis.^{22, 23}

Bladder involvement is frequent. The earliest manifestations are mucosal oedema and ulceration in surrounding of ureteric orifice. Bladder lumen appears irregular because of this ulceration and multiple tubercular granulomas. With advanced disease, cicatricial contraction of wall produces small bladder with multi-lobular shape and finally minute proportion bladder "the thimble bladder".²² In patients with unilateral non-functioning kidney, contracted bladder, and vesicoureteral reflux into the functional contralateral kidney. Now-days, CT scan is imaging modality of choice for GUTB. Over IVU, it provides extra information about adjacent adrenal, retroperitoneal space, prostatic and seminal vesicle abnormality. MRI is preferred in patients of compromised renal function, contrast allergy and pregnancy.

In our series calyces, infundibular irregularities were predominant renal findings. In ureter, lower ureteric stricture with proximal hydronephrosis is more common. In 8 patients of bladder involvement, 4 patients had contracted bladder.



CT KUB



Right Antegrade Study

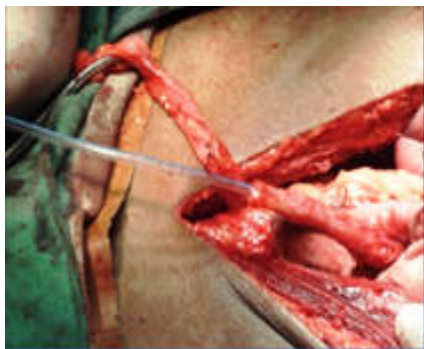
Cystoscopy most frequent findings are local hyperaemia, mucosal erosion and ulceration, tubercle formation, irregularity of the ureteral meatus and reduced bladder capacity. Bladder biopsy 18.5% to 52% sensitive. In our study, 8 patients had involvement of bladder, all were positive for bladder biopsy.

Short-course chemotherapy (SCC) is the standard of care for the treatment of TB.²³ Six-month regimens containing rifampicin and pyrazinamide are very effective with the fastest rates of culture conversion and the lowest rates of relapse. In India, DOTS implementation began in the year 1993 on a pilot basis. By March 2006, 100% coverage of the nation had been achieved. The treatment success rate has remained consistently above the global benchmark of 85%, and about 1.2 million lives have been saved. Standard Category I regimen is effective for the treatment of patients with GUTB.

Currently, there is no evidence to recommend the use of corticosteroids in the management of patients with GUTB. Same protocol was followed in our centre and 69.56 % patients who were positive for at least one urine test before the start of therapy became negative in three months. Despite availability of effective antitubercular therapy (ATT), surgery continues to play a role in management of GUTB.²⁴ A

minimum of four weeks of ATT is recommended before any major surgical intervention because it allows stabilization of the lesion and better planning of reconstructive surgery.²⁵

For renal and ureteral TB, stricture of pelvicalyces system is initially treated for drainage of hydronephrosis by ureteric stenting or percutaneous nephrostomy. The strictures should be monitored with CT or IVU. If there is deterioration or no improvement after six week period, then surgical reimplantation or other minimally invasive procedures including balloon dilatation may be necessary.



Caecocystoplasty Right Ileal Ureter, Left Ureteric Reimplantation

Intra op Pictures



Pouchogram- No Contrast Extravasation

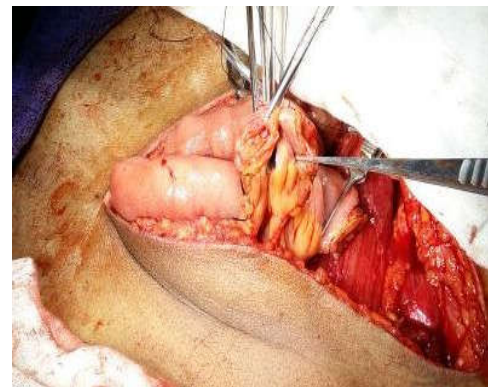
Partial nephrectomy is indicated for a localized polar lesion containing calcification that has failed to respond after six weeks of intensive chemotherapy; an area of calcification that is slowly increasing in size and threatening to gradually destroy the entire kidney. Traditionally, nephrectomy is strongly indicated in patients with a non-functioning tuberculous kidney with calcification or extensive disease involving the whole kidney with other complications including hypertension or co-existing renal cell carcinoma.

The indications for nephrectomy in a non-functional asymptomatic tuberculous kidney are still debatable, but most of the urologists are in favour of removing it. The indication for reconstructive bladder surgery is tubercular vesical contracture with frequency of micturition, vesicoureteral reflux and progressive hydroureteronephrosis.²⁵



Left Nephrectomy Intra OP Picture

Augmented cystoplasty should be considered in cases of non-compliant contracted bladders where non-operative management protocols have failed.²⁵



Augmentation Cystoplasty Using Ileal Loops

Surgical treatment should also be considered in tuberculosis of the testis or epididymis that shows persistent symptoms after administration of antituberculous agents.

In our study, 58.69% of patients underwent surgical intervention.

Limitations

The results of this study are subject to a few limitations. First, this study was conducted only with in-patients. This might have resulted in selection bias. Reliance on urinary PCR positivity, which may have high false positive rate, is another limitation. Lastly, comparisons between overall GUTB patients in the Indian population and enrolled patients in this study were not made. Further studies are needed to confirm.

CONCLUSIONS

Taken together, our results show that G.U.T.B occurred slightly more frequently in females and mainly in subjects in their third decade of life. It has delayed and various modes of presentation. A high index of suspicion is necessary and a wide range of investigations may be required to achieve a complete diagnosis of genitourinary tuberculosis. Multidrug chemotherapy combined with judicious surgery as and when indicated is the ideal treatment. Although short-term

antituberculous chemotherapy showed good treatment outcome with less adverse drug reactions but, unlike tuberculosis of other organs, >58% of the patients with G.U.T.B needed surgical treatment.

References

1. World Health Organization. Global tuberculosis control report, 2007. Available from: <http://www.who.int/tb/publications/global-report/2007/en/index.html>.
2. Vithalani N, Udani PM, Vithalani N. A study of 292 autopsies proved cases of tuberculosis. *Indian J Tuberc* 1982; 29: 93-7.
3. Marjorie PG, Holenarasipur RV. Extra-pulmonary tuberculosis: An overview. *Am Fam Physician* 2005; 72:1761-8.
4. Sharma SK, Mohan A. Extra-pulmonary tuberculosis. *Indian J Med Res* 2004; 120: 316-53.
5. Chattopadhyay A, Bhatnagar V, Agarwala S. Genitourinary tuberculosis in pediatric surgical practice. *JPediatr Surg* 1997; 32: 1283-6.
6. Wise GJ, Marella VK. Genitourinary manifestations of tuberculosis. *Urol Clin North Am* 2003; 30: 111-21.
7. Viswaroop BS, Kekre N, Gopalakrishnan G. Isolated tuberculous epididymitis: A review of forty cases. *J Postgrad Med* 2005; 51: 109-11.
8. Orakwe JC, Okafor PI. Genitourinary tuberculosis in Nigeria: A review of thirty-one cases. *Niger J Clin Pract* 2005; 8: 69-73.
9. Najjar MS, Bhat MA, Wani IA, et al. Profile of renal tuberculosis in 63 patients. *Indian J Nephrol* 2003; 13:104-7.
10. Medlar E M, Spain D M, Holliday R W. Postmortem compared with clinical diagnosis of genitourinary tuberculosis in adult males. *J Urology* 1949; 61:1078-88.
11. Kostakopoulos A, Economou G, Picramenos D, et al. Tuberculosis of the prostate. *Int Urol Nephrol* 1998; 30:153-7.t
12. Hemal A K, Aron M, Wadhwa SN. Auto prostatectomy; an unusual manifestation in genitourinary tuberculosis. *Br J Urology* 1998; 82:140-1.
13. Trauzzi S J, Kay C J, Kaufman D G. Management of prostatic abscess in patients with human immunodeficiency syndrome. *Urology* 1994; 43: 629-33.
14. Gow JG, Barbosa S. Genitourinary tuberculosis: A study of 1117 cases over a period of 34 years. *Br J Urology* 1984; 56: 449-55.
15. Wise GJ, Shteynshlyuger A. An update on lower urinary tract tuberculosis. *Curr Urol Rep* Jul 2008; 9(4): 305-13.
16. Singh SM, Wadhwa SN, Chhabra JS. The problems of genitourinary tract tuberculosis in India. *Indian J Surg* 1975; 37: 310.
17. Ginesu F, Pirina P, Sechi LA, et al. Microbiological diagnosis of tuberculosis: A comparison of old and new methods. *J Chemother* 1998; 10: 295-300.
18. Katoch V M. Newer diagnostic techniques for tuberculosis. *Indian J Med Res* 2004; 120: 418-28.
19. Negi S, Khan S F, Pasha St. Comparison of conventional diagnostic modalities, Bactec culture and Polymerase Chain Reaction Test for diagnosis of tuberculosis. *Indian J Med Microbiol* 2005; 23: 29-33.
20. Hemal A K, Gupta N P, Rajeev T P, et al. Polymerase chain reaction in clinically suspected genitourinary tuberculosis: comparison with intravenous urography, bladder biopsy, and urine acid fast bacilli culture. *Urology* 2000; 56: 570-4.
21. Premkumar A, Lattimer J, Newhouse JH. CT and sonography of advanced urinary tract tuberculosis. *Am J Roentgenol* 1987; 148: 659.
22. Suleman A. Tuberculosis of genito urinary system. *Ind J Radiol Imag* 1993; 3: 253-74.
23. Hong Kong Chest Service/British Medical Research Council. Five-year follow-up of a controlled trial of five 6-month regimens of chemotherapy for pulmonary tuberculosis. *Am Rev Respir Dis* 1987; 136: 1339-42
24. Rizzo M, Ponciotti R, Di Loro F, Scelzi S, Bongini A, Mondaini N. Twenty years' experience on genitourinary tuberculosis. *Arch Ital Urol Androl* 2004; 76: 83-7.
25. Duel BP, Gonzalez R, Bathold JS. Alternative techniques for augmentation cystoplasty. *J Urol* 1998; 159: 998-1005.

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