

Characteristics of genitourinary tuberculosis in Sri Lanka: A retrospective cohort study

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Abstract

Background

Although genitourinary Tuberculosis (GUTB) is the second commonest source of extrapulmonary TB in most countries, the reported rate of GUTB in Sri Lanka remains very low. Furthermore, the characteristics of GUTB in Sri Lanka have not been published due to paucity of data. Therefore, we aimed to study the clinical and imaging characteristics, treatment modalities and outcomes of GUTB in Sri Lanka.

Methods

A retrospective analysis was performed based on patients treated by a single urological surgeon in two consecutive centres over a period of 21 years. All patients (n=82, males = 45 (54.9%), median age: 51 years; range: 26 - 75) with a microbiological and/or histological diagnosis of GUTB were included. Median duration of follow-up was 24 months (range: 6- 96). Data were obtained from direct patient interview, hospital notes and clinic files.

Results

Commonest prominent symptoms at presentation included haematuria (n=13, 15.8%) and scrotal manifestations (n=12, 14.6%). Mantoux was either positive (>10mm) (n=62/70) or equivocal (>5mm) (n=8/70). Erythrocyte sedimentation rate (ESR) was available in 69 patients and was >30 in 54 (78.3%) patients. Chest x-ray and x-ray kidney-ureter-bladder (KUB) abnormalities were detected in 9 (11%) and 6 (7.3%) respectively. CT-urography was performed in 72 patients and abnormalities were detected in 57 (79%) patients. Forty-two patients underwent a cystoscopy and 73.8% (n=31) had abnormal findings. Microbiological diagnosis was feasible in 42 (51.2%) and rest were diagnosed histologically. Commonest organs involved were kidney (64.6%, n=53), ureters (51.2%, n=42), bladder (43.9%, n=36) and testis/epididymis (14.6%, n=12). One patient had prostate TB. All were treated primarily with anti-TB drugs however, 50 (61%) had indications for some form of therapeutic intervention. The majority of interventions were reconstruction surgeries (n=20, 24.4%) followed by excision surgeries (n=19, 23.2%) and drainage procedures (n=11, 13.4%).

Seven patients developed serious adverse reactions to anti-TB drugs. Five patients developed a thimble bladder and 3 patients developed end-stage renal failure. Two patients had relapse of infection.

Conclusion

CT-Urography, cystoscopy and histopathology are essential adjuncts to diagnose GUTB. Most ureteric strictures, non-functioning kidneys and epididymal masses needed surgical treatment. Long-term follow up is essential to detect progressive renal dysfunction.

Background

Tuberculosis (TB) is a major global health problem especially in the developing world [1]. In 2019, TB was one of the top ten leading causes of death. The recorded mortality was approximately 1.4 million including around 200,000 people with HIV [1]. The World Health Organization estimated an annual incidence of 9 million of which 95% are from the developing world. Extrapulmonary TB accounts for 15%-20% of reported cases [2, 3]. Among extrapulmonary TB, Genitourinary tuberculosis (GUTB) is the second commonest (20 to 40%) in most developed countries and the third commonest in most developing countries [2]. Moreover, GUTB is seen to coexist in around 2–20% of patients with pulmonary TB [3]. Miliary TB is believed to be the cause of GUTB where disseminated haematogenous spread is shown to occur in the genitourinary system in 25 to 60% of patients with GUTB [2]. Haematogenous seeding of primary TB infection to the kidney leads to granuloma formation which may subsequently caseate and rupture into the tubular lumen spreading to the distal urinary tract. The chronic and insidious nature of TB results in gradual damage to the genitourinary system by a combination of chronic inflammation, necrosis, abscess formation and scarring leading to direct injury or indirect injury secondary to obstruction [2, 3].

Sri Lanka is a South Asian tropical country with a population of 22 million. Although GUTB is the second commonest source of extrapulmonary TB in most countries, the reported rate of GUTB in Sri Lanka remains very low [4]. According to the National Programme for TB control and chest diseases (NPTCCD) data in 2007, only 4 GUTB cases were reported out of 1966 cases of extrapulmonary TB. Furthermore in 2019, only 59 GUTB cases were reported out of 2431 cases of extrapulmonary TB (8900 TB cases in total) [5]. This may be due to failure in case detection or deficiencies in proper reporting and documentation. In Sri Lanka, the characteristics of GUTB have not been published due to the paucity of data [4]. Only few case reports have been published describing rare manifestations of GUTB [6–9]. Knowing the disease characteristics is vital to establish early diagnosis and treatment and prevent chronic kidney disease. Therefore in this study, we aimed to study the clinical and imaging characteristics, diagnostic features, treatment modalities and outcomes of GUTB for the first time in Sri Lanka.

Methods

A descriptive retrospective cohort study was conducted at two tertiary care Urology Units in Sri Lanka, first in Karapitiya Teaching Hospital, Galle from 1.1.2000 to 30.11.2009 and subsequently from Colombo South Teaching Hospital, Dehiwala from 1.12.2009 to 30.6.2021 (a total period of 21 years) where the senior author worked. All patients with a diagnosis of GUTB, i.e TB involving the kidney, ureters, bladder, urethra, prostate, testis and epididymis were included in the analysis. All data were obtained from direct patient interview, hospital notes and clinic files. All data were recorded at the time of suspicion for GUTB and were followed up until diagnosis and completion of treatment. Ethical clearance was obtained from the Ethics Review Committee of the Colombo South Teaching Hospital.

Clinical characteristics including comorbidities, contact or past history of TB, clinical symptoms and signs, duration of symptoms were recorded. All patients underwent basic biochemical assessment including an erythrocyte sedimentation rate (ESR), and serum creatinine. Most patients underwent a Mantoux test (skin test for TB using purified protein derivative). An induration of ≥ 10 millimetres was recorded as a positive test in non-immunocompromised patients and ≥ 5 millimetres in immunocompromised patients [3]. However, a few patients did not undergo Mantoux test due to non-availability of reagents during that period. Ultrasound scan of the kidney, ureter, bladder and prostate (US-KUBP) and X-ray KUB was performed in all patients. Furthermore, patients with scrotal symptoms or signs underwent an additional scrotal ultrasonography. Computed tomography urogram (CTU) was performed in all patients except in those who presented with isolated scrotal symptoms and signs with negative US-KUBP and X-ray KUB. Abnormal findings noted in imaging were denoted according to the anatomical regions and involved organs.

Investigations such as urine for acid fast bacilli (AFB), urine for TB culture and polymerase chain reaction (PCR) were performed to obtain a microbiological diagnosis. However, in a subset of patients, some of these investigations were not performed due to non-availability of reagents and resources. Selective patients underwent a cystoscopy and bladder biopsy. Indications for cystoscopy included history of haematuria, lower urinary tract symptoms or ultrasonographic or CTU evidence of bladder abnormalities such as increased bladder wall thickness, contracted bladder, mass lesion in the bladder and the vesicoureteric junction. Bladder biopsy was performed in those with evidence of contracted bladder, mass lesion or inflammation of bladder epithelium. Histopathological findings obtained from cystoscopy and biopsy or percutaneous biopsies were recorded. A histological diagnosis GUTB was obtained in the presence of aggregates of epithelioid histiocytes, caseating necrosis and Langhans giant cells in the tissue specimen [10].

All patients were screened for pulmonary TB with a clinical assessment and mandatory chest X-ray and sputum AFB in those with a productive cough. TB of other regions were screened with a clinical history and examination of the lymph nodes and spine. Those with positive findings were subjected to further evaluation.

A diagnosis of GUTB was made in the presence of at least one of the following criteria in addition to clinical features: (1) at least 1 out of 3 urine samples positive for AFB using Ehrlich–Ziehl–Neelsen (EZN) technique. Three consecutive, early morning, mid-stream samples of urine were obtained for the test (2) positive urine or tissue culture for *Mycobacterium tuberculosis* complex (3) positive PCR for *Mycobacterium tuberculosis* complex, (4) tissue specimen showing histological evidence for TB such as chronic granulomatous inflammation with Langhans giant cells with or without caseation [3].

Patients were commenced on anti-TB therapy (ATT) as direct observed therapy (DOT) which is mandatory in Sri Lanka to enhance compliance and minimise default rate and lost to follow up. The adverse effects of ATT such as skin reactions and hepatotoxicity were also recorded. Hepatotoxicity due to ATT was defined as (1) at least a 5-fold elevation in alanine transaminase (ALT) and/or aspartate transaminase above the upper limit of normal (2) a >1.5 mg/dL increase in the total bilirubin level (3) clinical features of acute liver derangement such as loss of appetite, jaundice, vomiting, nausea, encephalopathy and at least a 3-fold elevation in ALT and/or AST levels [3].

Selected patients not responding to ATT or who developed anatomical complications such as stricture or abscess formation underwent invasive procedures. These include minimally invasive procedures such as percutaneous drainage, cystoscopy and stenting and open procedures such as open drainage and reconstructive surgical procedures. Data regarding treatment modalities such as anti-TB treatment (ATT), minimally invasive drainage procedures, cystoscopic intervention and open surgical procedures were recorded with their adverse effects and complications. Complications such as thimble bladder syndrome and progressive renal dysfunction were also recorded. Estimated GFR (eGFR) was used to measure renal function. Compared to the eGFR at diagnosis, an increase of eGFR $\geq 10\%$ at completion of treatment was defined as "recovery". An increase or decrease of 0–9% was defined as "stability" and a lowering of $\geq 10\%$ was considered as "deterioration" [3]. End stage renal disease (ESRD) was defined as eGFR less than 15ml/min/1.73 m² or requiring renal replacement therapy or transplant [11]. Thimble bladder syndrome was defined as disabling storage symptoms with bladder capacity of <150 ml as measured by filling the bladder with saline during cystoscopy.

All patients were seen six months after completion of ATT with US-KUBP and serum creatinine. Thereafter, those with structural abnormalities of the urinary tract in US-KUBP, high serum creatinine, single functioning kidney and those who had reconstructive surgery were followed up with annual US-KUBP and serum creatinine.

Statistical analyses were performed using SPSS software version 17. Data were expressed as frequency and percentages or median and range as relevant. Non-parametric tests were used to determine associations and statistical significance. Associations between categorical variables were determined using Chi-square test and associations between continuous and categorical variables were determined using Mann-Whitney U test. A p value of less than 0.05 was considered statistically significant.

Results

During the study period of 21 years, a total of 120 cases were suspected to have GUTB. However, after applying the diagnostic criteria mentioned above, 38 cases were excluded. Finally a total of 82 patients were included in the analysis.

Clinical characteristics

The majority were males (54.9%, n=45). The median age of the sample was 51 years (range: 26-75). The common presenting symptoms or reasons for referral to the urology unit were haematuria (n=13, 15.8%), scrotal mass/sinus (n=12, 14.6%), storage symptoms, urosepsis and dysuria (each 6.1%). The physical examination was unremarkable in the majority except in those with scrotal manifestations (n=12, 14.6%) and one patient had abdominal wall abscess. Three had a nodular prostate gland on digital rectal examination. Past history of TB or contact history of TB was positive in only 2 (2.4%) patients.

Basic investigations

Mantoux was performed in 70 patients and all were either positive (>10mm) (n=62, 88.6%) or equivocal (>5mm) (n=8, 11.4%). Strongly positive Mantoux (>15mm) was seen among 23 (32.9%). Only 18.2% of scrotal TB had strongly positive Mantoux whereas in others, 52.5% were strongly positive (p=0.036). ESR was available in 69 patients and was >30 and >50 in 54 (78.3%) and 33 (47.8%) patients respectively. The mean ESR was significantly lower in those with scrotal TB than others with abdominal manifestations (27 vs. 61, p=0.002).

Only 8 (9.8%) patients had elevated serum creatinine (>1.5mg/dl) at the time of diagnosis. Chest x-ray and x-ray KUB abnormalities were detected in 9 (11%) and 6 (7.3%) respectively.

CT-Urogram

CT-uogram was performed in 72 (87.8%) and abnormalities were detected in 57 (79.2%) patients. Isolated upper tract involvement was seen in 59.8% (n=49) and isolated lower tract abnormalities were detected in 3 (3.7%) patients. Another 3 (3.7%) patients had both upper and lower tract findings. Common findings at presentation were ureteric strictures (n=19 (26.4%), 15 were lower ureteric), non-functioning kidney (n=6, 8.3%), renal inflammation of abscess (n=7, 9.7%), stones or calcifications (n=6, 8.3%), contracted bladder (n=3, 4.2%) and masses (n=4, 5.6%) (Table 1).

Table 1
Summary of CT-uogram findings at the time of diagnosis

CT-Urogram findings		Total		Male		Female	
		N	%	N	%	N	%
Bilateral abnormalities	Yes	9	12.5%	7	20.0%	2	5.4%
	No	63	87.5%	28	80.0%	35	94.6%
Both upper and lower tract anomalies	Yes	3	4.2%	3	8.6%	0	0.0%
	No	69	95.8%	32	91.4%	37	100.0%
Only lower tract anomalies	Yes	3	4.2%	1	2.9%	2	5.4%
	No	69	95.8%	34	97.1%	35	94.6%
Only upper tract anomalies	Yes	49	68.1%	21	60.0%	28	75.7%
	No	23	31.9%	14	40.0%	9	24.3%
Ureteric stricture	Yes	18	25.0%	7	20.0%	11	29.7%
	No	54	75.0%	28	80.0%	26	70.3%
Renal stones	Yes	3	4.2%	2	5.7%	1	2.7%
	No	69	95.8%	33	94.3%	36	97.3%
Renal or ureteric calcification	Yes	3	4.2%	2	5.7%	1	2.7%
	No	69	95.8%	33	94.3%	36	97.3%
Small bladder	Yes	3	4.2%	3	8.6%	0	0.0%
	No	69	95.8%	32	91.4%	37	100.0%
Renal mass	Yes	3	4.2%	1	2.9%	2	5.4%
	No	69	95.8%	34	97.1%	35	94.6%
Bladder mass	Yes	1	1.4%	0	0.0%	1	2.7%
	No	71	98.6%	35	100.0%	36	97.3%
Non-functioning kidney	Yes	6	8.3%	2	5.7%	4	10.8%
	No	66	91.7%	33	94.3%	33	89.2%
Renal abscess	Yes	4	5.6%	2	5.7%	2	5.4%
	No	68	94.4%	33	94.3%	35	94.6%
Peri-renal abscess	Yes	2	2.8%	1	2.9%	1	2.7%
	No	70	97.2%	34	97.1%	36	97.3%
Spinal TB	Yes	2	2.8%	2	5.7%	0	0.0%
	No	70	97.2%	33	94.3%	37	100.0%
Psoas abscess	Yes	3	4.2%	2	5.7%	1	2.7%
	No	69	95.8%	33	94.3%	36	97.3%

Cystoscopy

Cystoscopy was performed only in those with lower urinary tract symptoms, haematuria, dysuria and in those with unclear diagnoses. Out of 42 patients who underwent a cystoscopy, 31 (73.8%) had abnormal cystoscopic characteristics that were further investigated by a bladder biopsy. Common predominant abnormality was inflamed bladder epithelium which was seen among 30 (71.4%) patients. Other anomalies included bladder or vesicoureteric mass (n=2), contracted bladder (n=2) and golf hole ureteric orifice (n=1). The histopathology was suggestive of TB in 25/31 patients (80.6%). All positive bladder biopsies had severely inflamed bladder epithelium.

Diagnosis

Microbiological diagnosis was achieved in only 42 (51.2%), whereas the rest were diagnosed histologically which included cystoscopy and bladder biopsy, percutaneous biopsy, open surgical biopsy or assessment of resected specimen. Only 6 patients had caseation in histology. Commonest organs involved were kidney (64.6%, n=53), ureters (51.2%, n=42), bladder (43.9%, n=36) and testis/epididymis (14.6%, n=12). Three patients with nodular prostate underwent trans-rectal ultrasound guided biopsy and only 1 patient had prostate TB. There were none with urethral TB.

Pulmonary and other extra-pulmonary manifestations

Four patients had concurrent pulmonary TB and other organ systems included psoas abscess (n=3), spine (n=2), anterior abdominal wall (n=1) and colon (n=1).

Treatment and follow up

All were treated primarily with anti-TB drugs however, 50 (61%) had indications for some form of intervention. Median duration of follow-up was 24 months (range: 6- 96). The preferred initial treatment was 2-month phase including four drugs, followed by a 4-months of maintenance with isoniazid and rifampicin. The majority of interventions were reconstruction surgeries (n=20, 24.4%) followed by excision surgeries (n=19, 23.2%) and drainage procedures (n=11, 13.4%). A summary of therapeutic interventions and their indications are given in Table 2. High ESR (>50) or positive Mantoux were not predictive of the need for therapeutic interventions (p=0.126 and p=0.744, respectively).

Table 2
Summary of therapeutic interventions and their indications

Type of intervention	N	Indications
Reconstructive Surgery (n=20, 24.4%)		
Ureteric reimplantation	14	Lower ureteric strictures (n=14)
Boari flap reconstruction	2	Lower and mid ureteric stricture (n=1) Lower ureteric stricture (n=1)
Uretero-ureterostomy	1	Upper ureteric stricture (n=1)
Resection of colovesical fistula tract and repair	1	Colovesical fistula (n=1)
Patient refused ureteric reimplantation	2	Lower ureteric stricture (n=2)
Excision Surgery (n=19, 23.2%)		
Nephrectomy	5	Non-functioning kidney (n=5)
Excision of epididymal mass	4	Epididymal mass (n=4)
Epididymectomy	4	Epididymal mass (n=4)
Orchidectomy	4	Large testicular/ epididymal mass (n=4)
Nephroureterectomy	2	Non-functioning kidney with a ureteric mass (n=1) Extensive nephroureteric calcification (n=1)
Drainage procedures (n=11, 13.4%)		
JJ stenting (via cystoscopy)	8	Lower ureteric stricture (n=3) Mild ureteric stenosis (n=2) Lower ureteric stricture with ureteritis cystica (n=1) Psoas abscess with hydronephrosis and hydroureter (n=1) Pyonephrosis (n=1)
Percutaneous nephrostomy	1	Pyonephrosis (n=1)
Guided aspiration	1	Renal abscess (n=1)
Open drainage (twice)	1	Psoas, peri-renal and anterior abdominal wall abscesses (n=1)

Drug toxicity

Seven patients (5 females and 2 males) developed significant drug toxicities. Six patients developed hepatitis with increased liver enzymes. All of them had discontinuation of isoniazid and rifampicin. Four patients had improvement of liver enzymes (ALT less than 50 U/litre in 2-3 weeks) after discontinuation therapy. Isoniazid and rifampicin were restarted and increased to full dose gradually without subsequent complications. In one patient, streptomycin, moxifloxacin and ethambutol was given during first three weeks (after stopping isoniazid and rifampicin) due to evidence of severe disease with a strongly positive Mantoux. One patient died of progressive liver derangement and liver failure in three weeks.

One patient developed extensive skin rash and itching and had low blood pressure without any evidence of hepatotoxicity. The patient was admitted and successfully treated with prednisolone and chlorpheniramine. Desensitization was performed successfully with gradual increment of drugs after two weeks under prednisolone cover.

Renal impairment

Eight patients had serum creatinine more than 1.5 mg/dl at the time of diagnosis (median: 2.4 mg/dl; range: 1.6 – 5.83). One patient had serum creatinine of 1.3 mg/dl at diagnosis that rose to 2.13 mg/dl and then came down to 1.7 mg/dl which was stable thereafter. One patient had normal creatinine at diagnosis that gradually rose to 3.2 mg/dl after 4 years. He is currently on an indwelling catheter for thimble bladder syndrome. Of the 8 patients with deranged creatinine at diagnosis, three had progressive deterioration of renal functions and two of them (one had thimble bladder) died of end stage renal disease while having renal replacement therapy in the form of haemodialysis (3 years and 5 years after starting ATT). One underwent a successful kidney transplant. Three and two patients each had "recovery" and "stability" of renal functions respectively.

Thimble bladder syndrome

Five patients (2 males and 3 females) had severe storage symptoms and bladder capacity less than 150 ml. One male patient died of progressive renal impairment and end stage kidney disease while being managed with an indwelling catheter. Another male is currently being followed up while on an indwelling catheter with a serum creatinine of 3.2 mg/dl. Both needed indwelling catheters to manage disabling storage symptoms. The three women were

managed without catheters. All refused bladder augmentation because of reluctance to perform clean intermittent catheterisation post-surgery. All were managed with antimuscarinic drugs such as oxybutynin or tolterodine.

Relapses

Two patients with relapsing disease were detected. One patient who was treated for renal TB presented with an epididymal mass and sinus formation after four years of treatment completion. Category two regime was given including streptomycin and the usual ATT.

Another patient who underwent nephrectomy for renal TB presented with severe haematuria, dysuria and frequency, 2 years after treatment completion. Cystoscopy showed severe inflammation of bladder epithelium and the bladder biopsy was positive. The patient was treated with ATT for 9 months. Streptomycin was avoided due to single kidney.

Discussion

We report our 21 years of experience in management of GUTB in a resource limited setting. Although we suspected TB in a much larger number of patients, only a smaller proportion of them were confirmed to have TB using the microbiological and histological criteria. These patients are at risk of progression of disease after ATT and thimble bladder and also progressive renal dysfunction. Mantoux > 15 mm was strongly predictive of active disease. Although granulomata with Langhans giant cells were seen in histology, caseation was rare. This may be due to effect of quinolones that are used liberally for patients with urinary symptoms. All ureteric strictures were treated with stenting and prednisolone. However, most ureteral strictures needed reconstruction such as uretero-ureterostomy or reimplantation. Most of drug toxicity was seen in females.

Interestingly, urethral and prostate involvement was extremely rare in our cohort. Although many urethral fistulae and masses were evaluated with biopsies and investigated for TB during the study period, none became positive for TB. Although prostate gland is less commonly involved, a number of cases of prostate TB has been identified in chippings after trans-urethral resection of the prostate in our neighbouring country - India [12]. However, we were able to detect only one patient during the last two decades. The reason for this regional variation seems unclear. In our cohort, around 15% of GUTB presented with scrotal manifestations such as a lump or rarely a sinus. In these patients, the positivity of ESR and Mantoux are significantly lower than those with abdominal manifestations. Therefore, high degree of suspicion and obtaining a tissue sample for further evaluation is mandatory to clinch the diagnosis.

Diagnosis of GUTB is a challenge due to the rarity of the disease and varying clinical presentation. Furthermore, basic imaging such as X-rays and ultrasonography are not reliable. X-ray KUB may show ill-defined or diffuse calcifications but this is becoming rare in the present and in our cohort such features were seen in only 7.3% [4]. Features in ultrasonography are also non-specific and may show calyceal dilatation, parenchymal destruction, calcification, hydronephrosis or collections [4]. However, it is not useful in most patients except in those with scrotal manifestations. CT-urogram was a useful investigation to detect anatomical abnormalities that are characteristic of TB such as ureteric stricture, unusual parenchymal calcification, non-functioning kidney etc [4, 13]. Cystoscopy and bladder biopsy was very useful in clinching the diagnosis in those with haematuria and lower urinary tract symptoms. Changes or inflammation, small capacity bladder, inflammatory masses and golf hole ureteric orifices were characteristic.

It is important to note that microbiological or histological confirmation is mandatory to start ATT due to the rarity of the disease and the potential side effects of ATT [14]. Starting ATT on clinical grounds without proper microbiological or histological confirmation should be discouraged as it may cause more harm. In our cohort, 7 patients developed serious adverse effects due to ATT and one patient died of liver failure. It is important to note that urine for AFB, Mantoux and granulomata are notorious to give rise to false positive results thus, use in isolation is not recommended by the experts [14]. Nevertheless, combination of these investigations is very useful to detect GUTB as TB culture or PCR may become negative with widespread usage of quinolones. Thus a combined effort of surgeons, radiologists, pathologists and microbiologists are required for the diagnosis [4].

Many patients required some form of intervention in addition to ATT for 6 months. However, six months of ATT may not be adequate in patients with a high burden of diseased tissue [14]. Unlike in pulmonary TB, Surgery in GUTB is an important adjunct [13]. Surgical procedures should be done after 4-6 weeks of anti TB therapy. Pus should be drained either through open or minimally invasive approach. Sinus formation after drainage of tuberculous abscess are not problematic and all healed with ATT. Extirpative/ excision surgery such as nephrectomy or orchidectomy is required in extensive disease not responding to ATT or when there is a suspicion of malignancy [13]. Reconstructive procedure was needed for almost all our patients with ureteric stricture as they did not respond to ATT and steroids. Although TB causes bladder fibrosis, ureteric reimplantations or Boari flaps were technically feasible with satisfactory healing as opposed to bladder fibrosis after radiotherapy. Bladder augmentation procedures are required for thimble bladder with disabling storage symptoms [13]. However, all five patients refused augmentation procedure as they did not prefer clean intermittent catheterization post-surgery. Finally, complex fistulae such as colovesical fistulae would need anatomical delineation followed by excision and reconstruction [13].

Prognosis of GUTB is satisfactory in general and in most patients, there was no evidence of impaired renal functions at the time of diagnosis. In those with elevated serum creatinine levels, most stabilised or recovered towards baseline with ATT. However, a minority developed end-stage disease especially in those with thimble bladder and bilateral renal involvement. We had three patients with ESRD and two died while on haemodialysis and one underwent successful renal transplant. Therefore, long term follow up is essential in patients with GUTB to identify those with progressive fibrosis and renal impairment. Relapses were uncommon after successful treatment completion.

We noticed several changes in the pattern of GUTB over the recent years. The number of cases are increasing in Sri Lanka. For example in 2007 only 4 cases while in 2019, 59 cases were reported [4, 5]. This may be due to increased awareness, detection and reporting. It may also indicate advancements in the facilities such as more availability of reagents for TB detection, availability of tests giving rapid results such as PCR and advanced nucleic acid replication tests – GeneXpert [14]. Since GeneXpert test is not recommended for urine, detection of acid-fast bacilli in urine smears was useful in the resource-limited

setting of ours [14]. Increased cases may be a reflection of increased prevalence of immunocompromised states in the Sri Lankan population such as diabetes and malignancies [15–17]. Multi drug resistance is becoming an emerging problem although it was not seen among our GUTB patients [14]. In Sri Lanka, an average of 16 patients with multi drug resistant TB per year among all detected TB cases has been reported during the period of 2018 to 2020 [5]. Fortunately, isolated GUTB is not contagious unlike active pulmonary TB and therefore, special isolation units are not required during the initial phase of treatment and patients can be treated as out-patients. The World Health Organization (WHO) has proposed the “End TB Strategy” to eliminate TB with a target of reduction of TB mortality by 95% and incidence by 90% by 2035 [18]. To achieve this goal, a high degree of suspicion and early case detection with prompt treatment is the way forward. Directly Observed Treatment (DOT) with polypills rather than individual drugs are implemented to enhance compliance and minimise default rate [14].

Limitations

There are several limitations in this study. This is a retrospective study based on patients treated by a single urological surgeon in two consecutive centres. However, we believe that our study is generalizable to most part of Sri Lanka as the institutions received referrals from a large catchment population throughout the island. As this is a resource limited setting, certain investigations were not carried out due to non-availability of facilities and reagents. Certain important data like presence of comorbidities like diabetes mellitus and other risk factors has not been recorded. Follow-up data is incomplete as information from patients who attended routine follow-up visits only have been collected. Nevertheless, this is a comprehensive report of two decades of experience and the first report of GUTB from Sri Lanka.

Conclusion

Best way to control TB is by high degree of suspicion and timely case detection and complete treatment. For this, diagnostic investigations in a large number of suspected patients is crucial. A combination of clinical and different investigations and an individualised decision based on a multi-disciplinary team is essential for the diagnosis of GUTB and there is no single easy gold standard test. Therefore, investigations such as CT-Urography, cystoscopy and histopathology are essential adjuncts to diagnose GUTB. Surgery is an important modality of treatment in most patients in addition to mandatory ATT. Follow up is needed after completion of ATT as some may progress to ESRD.

Abbreviations

TB
Tuberculosis
GUTB
Genitourinary tuberculosis
NPTCCD
National Programme for Tuberculosis control and chest diseases
AFB
Acid fast bacilli
EZN
Ehrlich–Ziehl–Neelsen
ESR
Erythrocyte sedimentation rate
ALT
Alanine transaminase
AST
Aspartate transaminase
US
Ultrasound
KUBP
Kidney Ureter Bladder Prostate
PCR
Polymerase chain reaction
CT
Computed tomography
ATT
Anti-TB treatment
eGFR
estimated glomerular filtration rate
ESRD
End-stage renal disease
SPSS
Statistical package for social sciences
DOT

Declarations

Ethics approval and consent to participate - Ethics approval for this study was obtained from the Ethics Review Committee of the Colombo South Teaching Hospital, Dehiwala, Sri Lanka. As this is a retrospective study and only anonymised previously collected data were analysed, no patient consent process was involved.

Consent for publication- As this is a retrospective study and only anonymised previously collected data were analysed, consent for publication was not obtained.

Competing interests – All authors declare that there are no competing interests

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Availability of data and materials- The data used in the above analysis will be available on reasonable request from the corresponding author.

Author's Contributions- UJ, MG and MW contributed to concept and design of study, acquisition of data, analysis, interpretation of data, drafting the article and final approval of the version to be published. SC, PU, CS and AA contributed to concept and design of study, revising it critically for important intellectual content; and final approval of the version to be published. AA is the senior author and guarantor of this paper.

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