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Original Article

Genitourinary tuberculosis in Taiwan: A 15-year experience at a teaching hospital

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Abstract *Background:* Genitourinary tuberculosis (GUTB) is rare but fatal if not diagnosed early. The purpose of this study was to investigate the outcomes of GUTB in Taiwan.
Methods: We retrospectively reviewed medical records of 57 patients who were diagnosed as GUTB from January 2002 to December 2016, over a 15-year period. Demographic data and clinical manifestations were recorded for analysis.
Results: There were 37 males and 20 females with a median age of 71 years. Kidney (24.6%) was the most involved organ. Fever (56.1%) was the major presentation. Sixteen (28.1%) patients presented unfavorable outcome. Compared with the favorable outcome group, the unfavorable outcome group had more malignancy ($p = 0.013$), fever ($p = 0.020$), anemia ($p = 0007$), thrombocytopenia ($p = 0.003$), and hypoalbuminemia ($p = 0.015$). In a

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multivariate analysis, fever (odds ratio: 42.716, 95% confidence interval: 1.032—1767.569; $p = 0.048$) was identified as prognostic factors for unfavorable outcome.
Conclusion: GUTB is often in advanced stages with a high mortality in Taiwan. Establishing a diagnosis is difficult and requires thorough investigation. Fever is associated with unfavorable outcome.

Introduction

Genitourinary TB (GUTB) accounted for only 1.0%—9.0% of newly diagnosed TB cases in Taiwan.[1,2] It has traditionally affected young and middle-aged individuals.[3—14] But in some studies, only 0%—4.1% patients were found to be young than 20 years.[3—5] GUTB can also cause serious urological complications, such as structural damage, loss of kidney function, and fatality if not diagnosed early.[3,6—8,15] Due to chronic and constitutional symptoms, the diagnosis of GUTB is often difficult and delayed,[3—5,8—11,16] with advanced cases reported in both Taiwan[4,10,16] and Spain.[11] Chang Gung Memorial Hospital-Chiayi (CGMH-Chiayi) is a 1300-bed tertiary teaching hospital in Chiayi, Southern Taiwan. Since Chiayi is an agricultural county, the patients at our hospital consist of primarily elderly individuals. Due to increase in older group, difficult to be diagnosed, often advanced disease with poor outcome when be diagnosed with GUTB, we conducted a 15-year retrospective study to explore the early diagnosis, the optimal treatment regimens, and outcome of GUTB. This retrospective study was approved by the Institutional Review Board of the Chang Gung Medical Foundation (Number: 96-1087B).

Materials and methods

Setting and study design

The medical records of patients that visited CGMH-Chiayi between January 2002 and December 2016 with a diagnosis of GUTB were reviewed. The following data was abstracted from the medical records: demographics, comorbidities, symptoms and signs, results of mycobacterial smears and cultures, histopathology, complete blood counts, serum biochemistry profile, radiographic scans, genitourinary tract operation(s), antituberculous chemotherapy, complications, and clinical outcomes. GUTBs were enrolled in the study if at least one of the following criteria was (were) met: 1) *Mycobacterium tuberculosis* complex (MTBC) was isolated from the genitourinary organ tissue or urine samples; and/or 2) the tissue of the genitourinary organs exhibited characteristic histologic evidence of caseating granulomatous inflammation, and the concomitant extra-genitourinary organ(s) showed positive culture(s) of MTBC.[3—10,17,18]

Disseminated TB was defined as the isolation of MTBC from extrapulmonary organs as follows: 1) two or more non-contiguous organs, or 2) one organ plus a histologic demonstration of caseating granulomatous inflammation in the bone marrow, liver, or another non-contiguous organ.[19]

The criteria of fever of unknown origin (FUO) selected were a febrile condition of more than three weeks' duration, a body temperature higher than 38.3 °C, and remaining under an uncertain diagnosis after one week of study in the hospital as proposed by Petersdorf and Beeson in 1961.[20]

Antimicrobial susceptibility testing

TB was diagnosed through the identification of MTBC by culture (Löwenstein-Jensen media). AFB staining was performed via Ziehl-Neelsen staining. Susceptibility testing agents included INH (0.2 μg), INH (1.0 μg), RIF, EMB (5 μg/mL), EMB (10 μg/mL), Ofloxacins, SM (2.0 μg/mL), and SM (10 μg/mL). The agar proportion method of susceptibility testing of MTBC was performed according to the guidelines proposed by the Clinical and Laboratory Standards Institute.[21]

Antituberculous therapy

First-line antituberculous drugs included isoniazid (INH) (4—6 mg/kg/day), rifampicin (RIF) (8—12 mg/kg/day), ethambutol (EMB) (15—20 mg/kg/day), and pyrazinamide (PZA) (15—30 mg/kg/day). The second-line antituberculous agents included streptomycin (SM) (15—20 mg/kg/day), kanamycin (15 mg/kg/day), amikacin (15 mg/kg/day), prothionamide (15—20 mg/kg/day), para-aminosalicylic acid (150 mg/kg/day), cycloserine (10—15 mg/kg/day), levofloxacin (7.5—10 mg/kg/day), moxifloxacin (400 mg/day), and rifabutin (5 mg/kg/day).[22,23]

Outcomes

Favorable outcome was defined as patients that completed antituberculous chemotherapy, the absence of symptoms/signs, and an absence of GUTB sequelae. Unfavorable outcome was defined as the mortality of patients expiring before diagnosis of GUTB or the completion of antituberculous chemotherapy.[24,25]

Statistical analysis

A multivariate logistic regression model was utilized to determine the potential risk factors for unfavorable outcome of GUTB. The Kaplan—Meier survival curve was

fitted into the Cox proportional hazard model. Categorical variables were tested using a Fisher's exact test, continuous variables were tested by a Student's t-test or Mann–Whitney U test, and a two-tailed p-value <0.05 was considered statistically significant. An odds ratio (OR) and 95% confidence interval (CI) were calculated to evaluate the strength of any association, as well as the precision of the estimate effect. All statistical calculations were performed using the Statistical Package for the Social Sciences for Windows (SPSS) Version 18.0 (Chicago, IL, USA).

Results

Patient characteristics

The data for 57 patients with GUTB were enrolled over a 15-year period. The median age was 71 years (range, 33–89 years) and the male to female ratio was 1.85 (37:20). The genitourinary organs involved were as follows: kidneys (n = 8), kidney and ureter (n = 4), epididymis (n = 3), epididymis and testis (n = 3), kidney and prostate (n = 2), prostate (n = 2), ureter (n = 1), ureter and bladder (n = 1), testis (n = 1), epidydymis and testis and prostate (n = 1), scrotum and penis (n = 1), and uterus and cervix (n = 1). A total of 21 (36.8%) patients had disseminated TB. The extra-genitourinary organs involved were as follows: the spines/peripheral joints (n = 18), bone marrow (n = 2), liver (n = 1), larynx (n = 1), peritoneum (n = 1), and lymph node (n = 1). However, 29 (50.9%) patients were diagnosed with GUTB according to positive urine MTBC after a series of examinations including physical examination, abdominal computer tomography, or abdominal sonography, but there was no clear confirmation of grossly infected genitourinary organs.

There were 49 (86.0%) patients that had associated comorbidities consisting of: 1) diabetes mellitus type II (20 patients, 35.1%); 2) chronic renal disease (19 patients, 33.3%), which included two patients receiving hemodialysis and one peritoneal dialysis; 3) underlying malignancies (14 patients, 24.6%), including five patients with hepatocellular carcinoma, three with prostate cancer, and one each with bladder, cervix, rectum, thyroid gland, lymphoma, and skin cancer; 4) adrenal insufficiency (14 patients, 24.6%); 5) corticosteroid use (12 patients, 21.1%); 6) chronic airway disease (11 patients, 19.3%); 7) liver cirrhosis (10 patients, 17.5%); 8) previous tuberculosis infection (9 patients, 15.8%), including the lung (n = 5), spine (n = 2), lung and spine (n = 1), and pleura (n = 1); 9) alcoholism (5 patients, 8.8%); and 10) autoimmune disease (2 patients, 3.5%). Thirty-three (57.9%) patients had more than two comorbidities.

Clinical manifestations and laboratory data

GUTB was diagnosed after admission in 50 (87.7%) patients. The median duration of symptoms between onset of symptoms and diagnosis was 4 months (range, 0.5–50 months). Forty-three patients (75.4%) exhibited systemic symptoms, and 41 (71.9%) patients presented genitourinary manifestations (Table 1). Fever (n = 32, 56.1%) was the most common symptom, followed by gross hematuria (n = 23, 40.4%). Of the biochemistry data, hypoalbuminemia (<2.5 g/dL) (n = 23, 40.4%) was most common, followed by anemia (<10 g/dL) (n = 16, 28.1%) (Table 2). Both pyuria (>20/high power field (HPF)) and hematuria (>30/HPF) (n = 17, 29.8%) were the most abnormal findings from the urine samples. Twelve (21.1%) patients had concomitant bacteriuria; *Escherichia coli* (n = 4) was the most common microorganism in the infected patients. Twenty-five (43.9%) patients had urolithiasis.

Table 1 Demographic and clinical characteristics with genitourinary tuberculosis (n = 57).

Characteristics	No. of patients (%)
Gender, male	37 (64.9)
Age distribution (years)	
30–39	1 (1.8)
40–49	4 (7.0)
50–59	11 (19.3)
60–69	9 (15.8)
70–79	17 (29.8)
80–89	15 (26.3)
Systemic symptoms	43 (75.4)
Fever	32 (56.1)
Malaise/fatigue	21 (36.8)
Weight loss	18 (31.6)
Night sweats	5 (8.8)
Genitourinary tract symptoms	41 (71.9)
Gross hematuria	23 (40.4)
Frequency/urgency	19 (33.3)
Dysuria	17 (29.8)
Flank pain	15 (26.3)

Mycobacteriology and chest röentgenograms

All specimens collected are listed in Table 3. Of the 57 cases in which MTBC was isolated from the genitourinary tissues (n = 9), urine (n = 50), sputum (n = 38), bronchoalveolar lavage (n = 6), bones and joints (n = 12), ascites (n = 1), or larynx (n = 1), 41 (71.9%) had positive smears for AFB. Of the nine patients with positive MTBC in

Table 2 Laboratory characteristics with genitourinary tuberculosis (n = 57).

Laboratory characteristics	No. of patients (%)
Hematologic & Biochemistry data	
Hypoalbuminemia (<2.5 g/dL)	23 (40.4)
Anemia (<10 g/dL)	16 (28.1)
Thrombocytopenia ($<150 \times 10^{12}$/L)	15 (26.3)
Urinary system related	34 (59.6)
Pyuria + hematuria	17 (29.8)
Isolated hematuria (>30/HPF[a])	10 (17.5)
Isolated pyuria (>20/HPF)	7 (12.3)
Microbiology	
Any drug-resistant MTBC[b] strain	7 (12.3)

Abbreviations: [a]HPF, high power field; [b]MTBC, *Mycobacterium tuberculosis* complex.

Table 3 *Mycobacterium tuberculosis* complex (MTBC) culture and acid-fast staining for specimens derived from 57 patients with genitourinary (GU) tract tuberculosis.

Culture specimens	No. of patients	MTBC − positive specimens	
		No. (%) of patients	No. (%) of positive AFB[a]
Any GU tract	56	55 (98.2)	26 (46.4)
GU tissue	10	9[b] (90.0)	4 (40.0)
Urine	53	50 (94.3)	22 (41.5)
Airway	52	39 (75.0)	22 (42.3)
Sputum	52	38 (73.1)	21 (40.4)
BAL[c]	8	6 (75.0)	2 (25.0)
Bones and joints	13	12[d] (92.3)	10 (76.9)
Ascites	7	1 (14.3)	0 (0)
Cerebrospinal fluid	6	0 (0)	0 (0)
Pleural effusion	4	0 (0)	0 (0)
Lymph nodes	2	0 (0)	0 (0)
Larynx	1	1 (100)	1 (100)
Any of the above	57	57 (100)	41 (71.9)

Abbreviations: [a]AFB, acid-fast bacilli; [b]including nine patients and ten sites (five epididymis, three testes, one kidney, and one uterus and cervix); [c]BAL, bronchoalveolar lavage; [d] including the spine (n = 9) and joints (n = 3).

Table 4 Histopathologic results for 57 genitourinary tuberculosis patients.

Biopsy site	No. of patients	
	Necrotizing granulomatous inflammation or caseous necrosis	Positive for AFB
GU	11	1
Testis	4	1
Ureter	3	0
Epididymis	3	0
Prostate	3	0
Kidney	1	0
Bladder	1	0
Uterus/cervix	1	0
Bone/joint	11[a]	0
Bone marrow	2	0
Larynx	1	0
Pleura	1	0
Lymph nodes	1	0
Liver	1	0

[a] Including the spine (n = 9) and elbows (n = 2).

the genitourinary tissue, only four had positive acid-fast smears for AFB in the tissue. From these 53 patients had urine cultures for MTBC, 19 urine cultures were analyzed for MTBC due to long-term genitourinary tract symptoms or disease recurrence following standard antibacterial therapy, 15 had possible disseminated TB, 14 had FUO, and the remaining five had other reasons.

Of the 57 patients with MTBC isolates, 50 (87.7%) were susceptible in vitro to first-line and second-line antituberculous agents, including INH, RIF, EMB, ofloxacin, and SM; 54 (94.7%) were susceptible to INH and EMB, 55 (96.5%) were susceptible to RIF, 53 (93.0%) were susceptible to SM, and one (multi-drug-resistant strain) to INH, RIF, EMB, and SM. Only one person had multi-drug resistant TB.

All patients underwent chest röentgenograms from which 31 exhibited radiographic evidence of pulmonary TB (PTB) and 25 (80.6%) had positive airway cultures; 26 were without obvious radiographic evidence of PTB; and 14 (53.8%) had positive airway cultures for MTBC.

Histopathology

Twenty-nine biopsies from the genitourinary tissues and extra-genitourinary sites were positive for necrotizing granulomatous inflammation or caseous necrosis in Table 4. One of the tissues from the testis above had a positive AFB smear.

Treatment

Of these patients, 37 (64.9%) underwent medical treatment only, 17 (29.8%) underwent medical therapy plus genitourinary tract surgery, 2 (3.5%) underwent no treatment, and 1 (1.8%) underwent only genitourinary tract surgery. Three patients who did not undergo medical treatment, because the diagnosis of GUTB was made after they expired. These 18 (31.6%) patients underwent genitourinary tract surgery, including a double J catheter stent insertion (n = 4), percutaneous nephrostomy (n = 3), orchiectomy (n = 3), epididymectomy (n = 2), ureterectomy (n = 2), ureteroscopy (n = 1), nephrectomy (n = 1), hydrocelectomy (1), and transurethral resection of a bladder tumor (1). Initially, 42 patients were administered a combination of four anti-TB treatments, and 12 patients underwent three combined treatments, including INH (5 mg/kg/day), RIF (10 mg/kg/day), and EMB (15–20 mg/kg/day) with/without PZA (20–25 mg/kg/day). There were 21 patients that had a total of 25 adverse events, including PZA-related hyperuricemia (n = 17), EMB-related blurred vision with suspected EMB related optic neuritis (n = 4), INH-related hepatitis (n = 2), and RIF-related cholestatic hepatitis (n = 2).

Outcomes

Of total 57 patients, 16 had unfavorable outcomes and 41 had favorable outcomes. These 16 (28.1%) unfavorable outcome group died of pneumonia with respiratory failure (n = 8), *Escherichia col*i septicemia (n = 3), heart failure (n = 2), methicillin-sensitive *Staphylococcus aureus* septicemia (n = 1), *Acinetobacter baumannii* septicemia (n = 1), and peritonitis (n = 1). The median treatment duration was 9.5 months (range, 6–26.5 months), and a median post-treatment follow-up duration was 30.3 months (range, 2–143 months) for the favorable outcome group.

The patients that experienced unfavorable outcome were also more likely to have malignancies (50% vs. 14.6%; $p = 0.013$), fever (81.3% vs. 46.3%; $p = 0.020$), anemia

Table 5 Univariate risk factors for favorable outcome and unfavorable outcome with genitourinary (GU) tuberculosis.

	Favorable (n = 41)	Unfavorable (n = 16)	*p*-value
Age, (years, mean ± SD[a])	67.4 ± 13.7	72.5 ± 13.1	0.200
Gender, male	29 (70.7)	8 (50)	0.216
Time to diagnosis (months, mean ± SD)	9.5 ± 11.7	4.7 ± 7.0	0.063
Disseminated disease	16 (39.0)	5 (31.3)	0.585
Comorbidities			
Diabetes mellitus	15 (36.6)	5 (31.3)	0.767
Chronic renal disease	12 (29.3)	7 (43.8)	0.356
Malignancy	6 (14.6)	8 (50)	0.013*
Corticosteroid use	9 (22.0)	3 (18.8)	1.000
Chronic airway disease	7 (17.1)	4 (25)	0.482
Liver cirrhosis	7 (17.1)	3 (18.8)	1.000
Previous tuberculosis	5 (12.2)	4 (25)	0.250
Alcoholism	4 (9.8)	1 (6.3)	1.000
Systemic symptoms			
Fever	19 (46.3)	13 (81.3)	0.020*
Weight loss	13 (31.7)	5 (31.3)	1.000
Night sweats	3 (7.3)	2 (12.5)	0.613
GU tract symptoms			
Gross hematuria	15 (36.6)	8 (50)	0.383
Frequency/urgency	15 (36.6)	4 (25)	0.537
Dysuria	15 (36.6)	2 (12.5)	0.109
Flank pain	11 (26.8)	4 (25)	1.000
Laboratory findings			
Anemia (<10/dL)	7 (17.1)	9 (56.3)	0.007*
Thrombocytopenia ($<150 \times 10^{12}$/L)	6 (14.6)	9 (56.3)	0.003*
Hypoalbuminemia (<2.5 g/dL)	12 (29.3)	11 (68.8)	0.015*
Microbiologic data			
MTBc resistant strains	4 (9.8)	3 (18.8)	0.388
MTBc eradication			
Any GU specimens	25 (61.0)	3 (18.8)	0.001*
Any specimens	31 (75.6)	4 (25)	<0.001*
GU tract surgery	17 (41.5)	1 (6.3)	0.011*

Abbreviations: [a]SD, standard deviation; Data is expressed as the number (%) of patients unless otherwise indicated. *: *p*-value <0.05.

(56.3% vs. 17.1%; $p = 0.007$), thrombocytopenia (56.3% vs. 14.6%; $p = 0.003$), and hypoalbuminemia (68.8% vs. 29.3%; $p = 0.015$). The favorable outcome group had a higher rate of any GU specimens MTBC eradication (61.0% vs. 18.8%; $p = 0.001$), any specimens MTBC eradication (75.6% vs. 25%; $p < 0.001$), and undergoing genitourinary tract surgery (41.5% vs. 6.3%; $p = 0.011$) (Table 5). In the multivariate analysis, any specimens MTBC eradication (OR: 0.007; 95% CI: 0.000–0.213; $p = 0.005$), and undergoing genitourinary tract surgery (OR: 0.000; 95% CI: 0.000–0.255; $p = 0.020$) were associated with favorable outcome, while fever had a negative impact odds ratio (OR: 42.716, 95% CI: 1.032–1767.569; $p = 0.048$) (Table 6). In Kaplan Meier survival analysis stratified with fever, it was shown that patients who suffered from fever had a significant lower survivorship for unfavorable outcome (Fig. 1).

Table 6 Multivariate regression for Unfavorable outcome with genitourinary (GU) tuberculosis.

	OR[a] (95% CI[b])	*p*-value
Malignancy	80.444 (0.703 −9208.865)	0.070
Fever	42.716 (1.032 −1767.569)	0.048*
Anemia (<10/dL)	18.673 (0.847 −411.463)	0.064
Thrombocytopenia ($<150 \times 10^{12}$/L)	4.676 (0.193 −113.133)	0.343
Hypoalbuminemia (<2.5 g/dL)	1.559 (0.130 −18.723)	0.726
Any specimens MTBC[c] eradication	0.007 (0.000 −0.213)	0.005*
GU tract surgery	0.000 (0.000 −0.255)	0.020*

Abbreviations: [a]OR, odds ratio; [b]CI, confidence interval; [c]MTBC: *Mycobacterium tuberculosis* complex, *: *p*-value <0.05.

Discussion

In Taiwan, the incidence of GUTB has decreased from 0.58 new cases per 100,000 in 2000 to 0.19 per 100,000 in

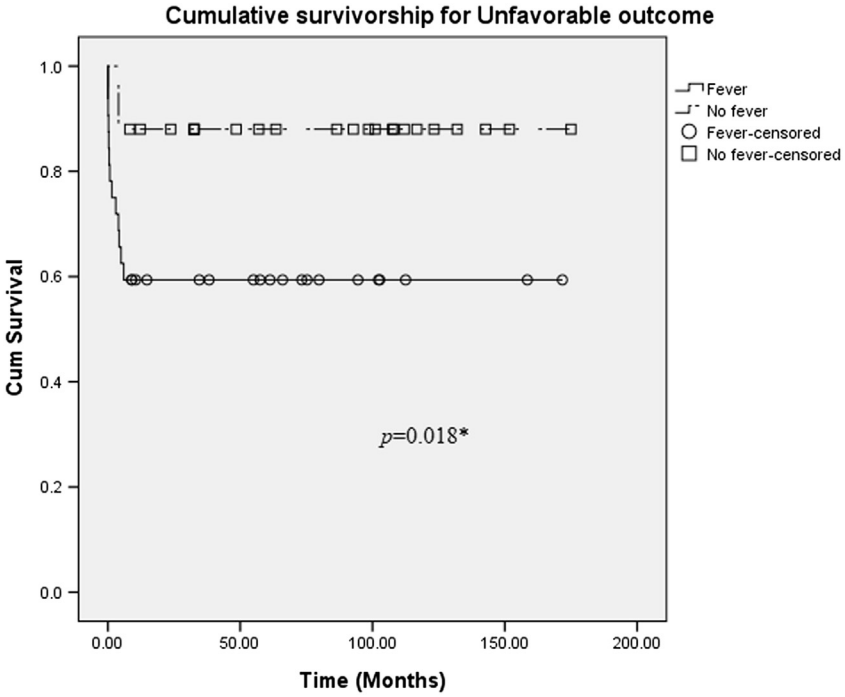

Fig. 1. Cumulative survivorship of unfavorable outcome stratified by fever.

2011.[1,2] GUTB has traditionally affected individuals with a mean age of 40.7 years.[3–14] In our study, only 1.8% of patients were younger than 40 years. In other studies in Taiwan, the mean age was 47 years in 1996[10] and 58 years in 2006.[4] GUTB seemed to be aging in Taiwan.

The constitutional symptoms of GUTB (9%–60.5%) include fever (7%–36%), malaise/fatigue (12.9%–17.3%), loss of body weight (7%–13.6%), and night sweats (3.2%–5.1%).[3,4,9–11,14] In Southern Taiwan, TB was diagnosed in 20.2% cases of FUO, including 11.7% cases of pulmonary TB and 8.5% cases of disseminated TB.[26] In addition, FUO in patients may alert physicians to consider the possibility of TB, especially in areas with high prevalence.[18] A total of 14 (24.6%) GUTB experienced FUO in our study. Fever and night sweats were more common in young adults than the elderly.[27] But our study reversed this result. Non-specific symptoms, such as an unexplained weight loss, fever, fatigue, or weakness may be an indication of TB, therefore, GUTB may present with these GU-specific symptoms.[18,28] So, we think that GUTB was necessary in agricultural county if patients unexplained non-specific symptoms including FUO.

The symptoms of GUTB (80%–93.6%) include dysuria (32.4%–67.9%), frequency or urgency (34.4%–63.0%), gross hematuria (7.9%–53.3%), and flank pain (10%–67%).[3–5,7–14,18] Moreover, GUTB is associated with an abnormal urinalysis (84%–93%), including isolated pyuria (18%–46%), and isolated hematuria (4%–12.9%).[4,9–11] In patients with GUTB, lower genitourinary tract symptoms were reported to be more frequent than constitutional symptoms.[9,13] In contrast to these studies, more constitutional symptoms (75.4%), fewer focal symptoms (71.9%), and fewer urinary abnormalities (59.6%) were found in our study. These clinical and laboratory manifestations were atypical presentations of GUTB, so these phenomena increased the difficulty of diagnosis of GUTB. In GUTB, one study proposed the median duration between the onset of symptoms and diagnosis of GUTB was two months,[4] compared to the four months in our study. Unlike previous studies, our patients had longer clinical symptoms before they were diagnosed of GUTB. In other words, more patients were delay diagnosed. However, the delayed diagnosis of TB can lead to increased morbidity and mortality in elderly individuals.[27] This discrepancy may be due to the older median age and number of comorbidities in our study. About involved organs of GUTB, the most commonly involved organs were still the kidneys in both previous studies (42.6%–74.8%)[8,9,16] and in our study (24.6%). However, the percentage of GUTB patients without grossly infective genitourinary organs was more than half (50.9%) and higher than one study in Northern Taiwan (41%).[16] We were more surprised that more than one-third of GUTB patients had been diagnosed with disseminated disease than previous studies (27.9%).[16] In addition, GUTB was more disseminated and advanced disease when be diagnosed with GUTB in our study (36.8%) than that reported by another study (27.9%) in Taiwan.[16] Fewer definite infected genitourinary organs were challenging for the diagnosis of GUTB.

In the study conducted by Bentz et al.,[29] 6.7% patients with a positive urine culture for *M. tuberculosis* had no current genitourinary symptoms. The lack of genitourinary symptoms, and a urinalyses within the normal limit cannot exclude the possibility of GUTB.[29] Approximately 4.9%–43.1% patients with GUTB have a concomitant bacterial urinary tract infection (UTI).[4,10,11,13,14] Thus, a co-existing

bacterial UTI may mask the underlying GUTB.[13] If standard therapy for recurrent disease is ineffective, GUTB should be taken into account of a differential diagnosis.[8,13]

According to the literature, positive MTBC airway specimens were obtained in 31.6%–37.2% patients,[5,13] whereas 75.0% patients were identified in our study. This result may be due to the majority of elderly patients being treated at our hospital, and Chiayi has a high TB incidence. PTB was identified via chest radiography in 14%–58.6%,[3–5,9–11,13,14] and 54.4% cases in our study, respectively. There were 14 (53.8%) out of the 26 patients without obvious radiographic evidence of PTB that were airway positive for MTBC. Routine chest radiographs plus airway specimens are mandatory to detect concurrent PTB in GUTB in a high prevalence country.

At least one positive urine culture for MTBC is necessary for establishing a definitive diagnosis and an early diagnosis of GUTB.[3–10,13,14,17,18] Approximately 25.2%–90.8% of GUTB patients were urine positive for MTBC in the literature,[3–5,7–10,13,14] and 94.3% were positive in our study. In a study of patients with suspected PTB conducted by Gopinath et al.,[30] 56.8% were positive for airway specimens MTBC cultures, however 18.5% were positive for urine MTBC cultures. The most useful approach for diagnosing an MTBC infection was to obtain cultures from all body fluids and tissues.[18] The examination of urine culture for MTBC had many advantages. Urine was easier to pick up and, less contaminated, and we could get obtain more volumes of urine specimen than sputum when we collected these specimen. These patients could collect urine by himself and performed at the outpatient department. Regarding to costs, urinary culture for tuberculosis is cheaper than other diagnostic methods including TB PCR, QuantiFERON-TB Gold In-tube test, biomarker, and liposomal agglutination-based method.[31–35] So, morning urine cultures for MTBC were a useful tool for confirming suspected EPTB and FUO in our study.[29]

Moreover, there was a higher mortality (28.1%) in our study compared to GUTB (1.2%–14.7%) in the literature.[6,10–12,16] The crude mortality rate of GUTB increased significantly. The treatment success rate of GUTB in Taiwan may be lower for elderly patients and those who have multiple comorbidities, associated with a high morbidity for patients with GUTB.[4,16] Because of multiple comorbidities (86.0%), more elderly patients (median age 71 years old) and delay diagnosis, our study had poor outcomes. In our study, the multivariate regression (Table 6) showed that unfavorable outcomes for GUTB were poor any specimens MTBC eradication, and without GU tract surgery. Fever was an unfavorable outcome (Fig. 1) and this was probably due to highly associated with FUO, very older patients, and multiple underlying illnesses. In addition, patients with multiple positive urine cultures may have a somewhat higher relapse rate following complete chemotherapy.[15,17] On the other hand, the favorable outcome group was associated with a significantly sterilization of the genitourinary tract cultures (61.0% vs. 18.8%) and any of the other specimens (75.6% vs. 25.0%) compared to those for unfavorable outcome group. According to the results of our study, it is very important to perform follow-up specimen cultures every month for MTBC until sterility is achieved after the initiation of antituberculous chemotherapy, to predict treatment outcome. The result of sputum culture, which changed from culture-positive to culture-negative, was an important assessment of the successful treatment of pulmonary tuberculosis. According to our study, any specimens MTBC eradication had a favorable outcome. So we suggested that it was important to regular follow-up of any specimens of MTBC eradication until the culture was negative. But the frequency and intervals of the culture of specimens needed more studies.

Medical treatment rather than surgery is the priority for GUTB.[3,10,11,16,36] However, surgical intervention may be helpful in some complicated cases, such as hydronephrosis, neoplasia formation, or to prevent permanent sequela.[3,6,10,11,13,36] In previous studies, 3.3%–70.7% of GUTB patients underwent surgery,[4,6–8,10–12,14,16] and our study is within this range (31.6%). However, therapeutic surgical intervention could not replace antituberculous chemotherapy. Because of the intervention of earlier genitourinary surgery could reduce the bacteria load of tuberculosis and decreased complications. In GUTB, the favorable outcome group treated group had a significantly higher rate of genitourinary tract surgery (41.5% vs. 6.3%). In our results, we suggest therapeutic genitourinary operation is necessary if the effect of anti-tuberculous medication is unfavorable. However, larger studies are warranted to confirm this association.

The diagnosis of GUTB requires a high level of alertness, which remains a challenge to clinicians (5). Once GUTB is diagnosed, treatment should be initiated as early as possible to prevent serious complications.[6,18]

The present study was limited by the small number of patients and its retrospective nature. However, the occurrence of GUTB was not common, involving only 57 patients over a 15-year period. Meanwhile, the present study included patients were all older than 33 years old. GUTB in our study was diagnosed mainly based on MTBC cultures but not by routine polymerase chain reactions. This is another limitation.

In summary, this study demonstrated the following important points: 1) the diagnosis of GUTB is difficult and it often occurs in individuals older than 40 years with a male predominance, disseminated, febrile, multiple comorbidities, and high mortality; and 2) patients with anemia, without genitourinary surgery, and persistence MTBC cultures of any specimens are associated with poor outcomes.

Conflicts of interest

None declared.

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