Original Research Article

Incidence and epidemiological features of urogenital tuberculosis among adult inhabitants in Qatar

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ABSTRACT

Background: Urogenital tuberculosis (UGTB) has not been extensively studied in the Gulf region, particularly in Qatar. This study aimed to describe the incidence, demography, presentation, diagnosis, and treatment outcomes of UGTB among adult patients in Qatar.

Materials and Methods: This retrospective descriptive study was conducted from January 1, 2015, to December 31, 2020, in six centers of Hamad Medical Corporation in Qatar. All patients with UGTB admitted or treated at these centers were included in the study.

Results: During the study period, we recruited 106 patients with isolated or combined UGTB, representing 0.4 percent of all TB cases and an incidence of 0.7 new UGTB cases per 100,000 population in Qatar between 2015 and 2020. Most patients were males [79 (74.5%)] and non-Qataris [102 (96.2%)]. The mean age of the patients was 40.60 ± 11.39 years. The mean illness duration was 86.98±129.84 days, and the most frequent presenting symptom was abdominal pain [51(48.1%)]. UGTB was diagnosed by direct bacilli identification or culture growth in 34 (32.1%) patients; histopathology in 55 (51.9 %) patients; and a combination of strong clinical, laboratory, and radiographic evidence of UGTB without microbiological or histological confirmation in 17 (16.0%) patients. All patients received anti-tuberculosis therapy with various durations, while surgical interventions were reported in 73(68.9%) cases. Most patients, 85 (80.2%), completed their treatment in Qatar, while 21 (19.8%) left the country before completion, and no mortalities had been reported.

Conclusion: The diagnosis of UGTB is generally delayed due to vague clinical features. Awareness of UGTB is essential for physicians to suspect this disease in patients with unexplained urogenital symptoms, especially in patients from TB-endemic areas or with a history of pulmonary tuberculosis.

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1. Introduction

Tuberculosis (TB) is one of the top ten causes of death globally and is a major public health concern causing significant physical and psychosocial morbidity. In 2022, TB was the second leading cause of death from a single infectious agent worldwide, after coronavirus disease (COVID-19). TB continues to affect more than 10 million people each year, with most new TB cases occurring in the Southeast Asia region (46%), followed by the African region (23%) and the Western Pacific (18%).[1,2] About 87% of new TB cases occurred in the 30 high-

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burden countries, with Bangladesh, China, the Democratic Republic of Congo, India, Indonesia, Nigeria, Pakistan, and the Philippines accounting for more than two-thirds of the global total TB cases.[2] Despite major efforts to increase detection, an estimated third of new TB cases are still missed each year. The unavailability of a rapid, low-cost, accurate diagnostic assay that can be used at the point of care is a major hindrance.[3]

Urogenital tuberculosis (UGTB) refers to an infectious inflammation of any urogenital organ, isolated or combined,[3] representing 30 to 40% of cases of extrapulmonary tuberculosis worldwide.[3,4] UGTB is an insidious disease in which symptoms are generally recognized late, leading to delayed diagnosis with subsequent destruction of the urogenital organ.[3] Diagnosis is difficult because it does not have specific clinical features and hides under the mask of other diseases, most often urogenital tract infections, cancer, and urolithiasis.[4] Few studies have been conducted on UGTB, likely due to unclear diagnostic criteria and treatment recommendations.[3,4]

In Qatar, TB remains a common health problem. Although the number of TB infections in Qatar declined to 37 cases per 100,000 population in 2022, the last two years recorded a significantly higher number of TB infections than the preceding years.[5] A retrospective population-based study showed extrapulmonary TB accounted for 53.6% of all TB cases in Qatar with UGTB accounting for 1.4% of cases of extrapulmonary TB.[6] However, there is a lack of information about UGTB in Qatar as UGTB has not been studied in detail. The present study was undertaken to describe the incidence, demography, presentation, diagnosis, and treatment outcomes of UGTB among adult patients in Qatar.

2. Materials and Methods

2.1. Study design, setting, and population

This retrospective descriptive study was conducted from January 1, 2015, to December 31, 2020, in six centers of Hamad Medical Corporation in Qatar, specifically Hamad General Hospital, Al Wakra Hospital, Al Khor Hospital, Hazm Mebaireek General Hospital, and Women's Wellness and Research Center, and the Communicable Disease Center (CDC). All patients with urogenital TB (UGTB) admitted or treated at these centers were included in the study.

2.2. Definitions, exclusion/inclusion criteria, diagnosis of UGTB cases

Throughout our study, we adopted the following definitions for UGTB:[7]

2.2.1. Urological tuberculosis (UTB)
tuberculous infection of the organs of the urinary system in female patients and isolated or in combination with the genital system in male patients, caused by Mycobacterium TB or Mycobacterium bovis.

2.2.2. Genital tuberculosis (GTB)
tuberculous infection of the female or male genitals, caused by Mycobacterium TB or Mycobacterium bovis.

2.2.3. Urogenital tuberculosis (UGTB)
tuberculous infection of urogenital system organs isolated or in any combination, caused by Mycobacterium TB or Mycobacterium bovis.

2.2.4. Inclusion and exclusion criteria
All consecutive patients aged 18 years or older who were diagnosed with UGTB were included in this study. Patients with tuberculosis (whether pulmonary or extra pulmonary) who did not have confirmed findings of tuberculosis in the genitourinary tract, patients less than 18 years old, or patients who had missing data were excluded.

2.3. Diagnosis of UGTB

In this study, the diagnosis of UGTB was made by the treating physicians based on clinical symptoms and at least one of the following conditions:

1. Ziehl-Neelsen stains, polymerase chain reaction (PCR), or Lowenstein cultures of urogenital specimens were positive for TB.
2. Evidence of caseous necrotic granulomas in urogenital tissue specimens.
3. Combination of strong clinical, laboratory, and radiologic evidence of urogenital tuberculosis without microbiological or histological confirmation plus clinical improvement after empirical antituberculosis therapy.

2.4. Sample size and sampling strategies

Our study was conducted on the entire group of patients with UGTB diagnosed during the study period (complete enumeration), and a purposive sampling strategy was followed for sample selection.

2.5. Case identification and data collection

All cases of TB infection in Qatar, including UGTB, are treated exclusively in Hamad Medical Corporation, so this study can be considered a population-based study. Detailed data on patients with UGTB were obtained from electronic medical records (Cerner). Demographic data, information on disease location, clinical presentation, presence of

comorbidities, microbiological and histopathological findings, and outcomes were collected.

2.6. Statistical analyses and ethical approval

Descriptive data analysis was performed with SPSS software (v 23; IBM Corp, Armonk, NY, USA). All relevant data were reported as means standard deviation (SD) for quantitative variables, while qualitative variables were described as numbers and percentages.

The incidence of UGTB in this study was calculated as the number of reported UGTB cases (during the study period) divided by the total population aged 18 years or older during the same period multiplied by 100,000. This study was approved by the Ethics Committee of Hamad Medical Corporation (Protocol Number: MRC-01-21-989).

Table 1: Demographic characteristics of the patients involved in this study.

Variable	N(%)
Age [MeanSD(range)]	40.6011.39(20-72 years)
Sex	
Male	79(74.5)
Female	27(25.5)
Nationality	
Indian	24(22.6)
Nepalese	16(15.1)
Bangladeshi	16(15.1)
Pakistani	14(13.2)
Filippino	10(9.4)
Egyptian	7(6.6)
Ethiopian	4(3.6)
Kenyan	4(3.6)
Qatari	4(3.6)
Ugandan	2(1.8)
Moroccan	1(0.9)
Sri Lankan	1(0.9)
Afghani	1(0.9)
Eritrean	1(0.9)
Indonesian	1(0.9)

3. Results

3.1. Demographics of the participants

During the study period, we recruited 106 patients with isolated or combined UGTB, representing 0.4 percent of all TB cases and an incidence of 0.7 new UGTB cases per 100,000 population in Qatar between 2015 and 2020. Most patients were males [79 (74.5%)] and non-Qataris [102 (96.2%)]. The mean age of the patients was 40.60 11.39 years (20–72 years). Table 1 summarizes the demographic characteristics of the patients involved in this study.

Table 2: Clinical characteristics of the patients involved in this study.

Clinical presentation	N(%)
Fever	43(40.6)
Cough	11(10.4)
Night sweat	24(22.6)
Anorexia/weight loss	24(22.6)
Primary infertility	11(10.4)
Back/flank pain	24(22.6)
Abdominal pain	51(48.1)
Pelvic pain	6(5.7)
Dysuria	49(46.2)
Frequency	34(32.1)
Hematuria	39(36.8)
Pyuria	35(33.0)
Nocturia	14(13.2)
Urinary tract obstruction	9(8.5)
Renal impairment	7(6.6)
Irregular menstruation	7/27 (25.9)
Enlarged kidney	11(10.4)
Abscess with fistula	15(14.2)
Bloody ejaculation	2/97
Vaginal bleeding/discharge	2/27(7.4)
Testicular swelling	38/97(39.2)
Lymphadenopathy	6(5.7)
History of TB	
History of contact	17(16.0)
Past history of TB	6(5.7)
Family history of TB	7(6.6)
Duration of illness [MeanSD(range)]	86.98129.84 (range:17-730 days)
Comorbidity	
Diabetes mellitus	23(21.7)
Hypertension	14(13.2)
Chronic kidney disease	5(4.7)
Malignancy	5(4.7)
Transition Cell Carcinoma	4(3.6)
Lymphoma	1(0.9)
Immune suppression	1(0.9)
QuantiFERON-TB Gold test	N=95
Positive	67(70.5)
Nonconclusive	4(4.2%)
Negative	24(25.3%)
Extra-urogenital TB	N=8
Lung	8(100)
Lymph nodes	6(75.0)
Peritoneum	2(25.0)

Table 3: Urogenital organ involved in this study

Urogenital organs	N(%)
Isolated UGTB	
Urological TB	45(42.5)
Epididymo-orchitis TB	41(38.7)
Isolated Prostate TB	2(1.9)
Ovary	7(6.6)
Uterus	5(4.7)
Combined UGTB	
Urological/Prostate TB	4(3.8)
Urological/Prostate/ Epididymo-orchitis TB	2(1.9)
Total	106

UGTB: Urogenital tuberculosis

Table 4: The histopathological and microbiological results from different biopsies from patients involved in this study

Specimen/sample	Number of tests performed	AFB smear positive (%)	PCR positive (%)	TB culture positive (%)	Caseating granuloma positive (%)
Urine	47	19(40.4)	24(51.1)	24(51.1)	NA
Renal biopsy	3	ND	ND	ND	3(100)
Aspirate (abscess/discharge)	13	8(61.5)	8(61.5)	10(76.9)	NA
Ureter biopsy	3	ND	ND	ND	2(66.6)
Lymph node biopsy	6	ND	ND	ND	6(100)
U bladder biopsy	21	4(19.1)	ND	ND	11(52.4)
Epididymal/testis biopsy	40	5(12.5)	ND	ND	30(75.0)
Prostate biopsy	5	ND	ND	ND	3(60.0)
Ovarian biopsy	3	ND	ND	ND	3(100)
Endometrial biopsy	3	ND	ND	ND	3(100)
Peritoneal biopsy	2	ND	ND	ND	2(100)
Sputum	14	6(42.9)	6(42.9)	8(57.1)	NA

ND: not done; NA: not applicable

Table 5: Treatmentand outcomes of UGTB

Variable	N(%)
Anti-TB treatment	99(93.4)
4-drug	7(6.6)
2nd line treatment	
Duration of anti-TB therapy [MeanSD(range)]	3.043.69(1-12 months)
Surgical intervention	
Double J-stent insertion	9(8.5)
Nephrostomy	9(8.5)
Nephrectomy	3(2.8)
Abscess drainage	13(12.3)
Transurethral resection of prostate	5(4.7)
Oophorectomy/salpingectomy	3(2.8)
Epididymectomy	40(37.7)
Outcome	
Cured	85(80.2)
Left before treatment completion	21(19.8)

Anti-TB: anti-tuberculosis

3.2. Comorbidities and the clinical characteristics of the participants

Comorbidities were identified in 47 (44.3%) cases, with diabetes mellitus being the most common at 23 (21.7%), while a history of contact with tuberculosis patients was identified in 17(16.0%) cases. The mean illness duration was 86.98129.84 days (range:17-730 days), and the most frequent presenting symptom was abdominal pain [51(48.1%)], followed by dysuria [49(46.2%)], fever [43(40.6%)], and hematuria [39(36.8%)]. The most common sign was testicular swelling [38/97(39.2%)]. QuantiFERON-TB Gold in-tube assay with the peripheral blood was performed in 95(89.6%) patients; it was positive in 67(70.5%) cases, while it was inconclusive in 4(4.2%) cases and negative in 24(25.3%) cases. Table 2 describes the clinical characteristics of the participants. UGTB was observed to involve an isolated organ or in any combination with other UG organs (Table 3).

3.3. Diagnosis of UGTB

UGTB was diagnosed by direct bacilli identification or culture growth in 34 (32.1%) patients; histopathology in 55 (51.9 %) patients; and a combination of strong clinical, laboratory, and radiographic evidence of urogenital tuberculosis without microbiological or histological confirmation in 17 (16.0%) patients. Table 4 summarizes the histopathological and microbiological results for different biopsies taken from patients involved in this study.

3.4. Treatment of UGTB and outcomes

All patients received anti-tuberculous therapy with various durations. Most patients [99(93.4%)] received a 4-drug antituberculosis regimen (Isoniazid, Rifampicin, Ethambutol, Pyrazinamide), while only 7(6.6%) patients received second-line anti-tuberculous therapy (linezolid, moxifloxacin, amikacin, levofloxacin). The mean treatment duration was 3.043.69(range:1-12 months). Surgical interventions were reported in 73(68.9%) cases, including Double J-stent insertion, nephrostomy, nephrectomy, abscess drainage, transurethral resection of prostate, Oophorectomy, salpingectomy, and epididymectomy. Most patients, 85 (80.2%), completed their treatment in Qatar, while 21 (19.8%) left the country before completion, and no mortalities had been reported. Table 5 describes the treatment and outcomes of UGTB in our cohort.

4. Discussion

There are few studies on UGTB, probably due to the challenges in making an accurate diagnosis arising from the diverse and nonspecific clinical presentations, a lack of clinical awareness of the possibility of TB, and the presence of other comorbidities such as HIV, diabetes, and bacterial urinary tract infections.[8] Therefore, the exact incidence of UGTB is unknown. Yet, our study found that the incidence of UGTB was estimated to be 0.7 new cases per 100,000 population, accounting for 0.4% of total TB cases observed in Qatar during the study period.

In Qatar, TB is a notifiable disease. All cases of tuberculosis must be notified to the Communicable Disease Control and Prevention Section of the National Health Authority, however, there is a lack of data on UGTB. To our knowledge, our study was the first to describe UGTB in Qatar. As noted in Table ??, our study showed that UGTB predominantly affected male patients in their 40s and from high TB prevalence countries, which is comparable to other UGTB cohort studies.[9–12] The illness primarily impacted expatriates who likely contracted it in their home country and experienced reactivation upon or after moving to Qatar, possibly due to stress and poor socioeconomic conditions upon arrival that improved over time. In contrast, Qatari residents likely caught the disease during childhood (through travel to countries with higher prevalence or contact with affected individuals) and experienced reactivation later in life.[13]

UGTB is an insidious disease where diagnosis is generally delayed due to vague clinical features and a low index of suspicion. In this study, certain patients were unexpectedly diagnosed with UGTB while undergoing diagnostic evaluations for other health issues. For instance, 11 (10.4%) individuals had been under the care of their primary care doctors for primary infertility and were later found to have UGTB following several months of diagnostic tests. Moreover, 9 (8.5%) patients were under the care of a urology team for obstructive uropathy and were ultimately diagnosed with UGTB after thorough diagnostic evaluations. The mean illness duration in our study was 86.98129.84 days (range:17-730 days).

UGTB has no specific pathognomonic clinical features. It may appear with various clinical presentations, ranging from having no symptoms through subclinical, non-specific symptoms and signs, to obstructive uropathy and renal impairment. In our study, abdominal pain was the most common presenting symptom, which is comparable with other studies[9,14,15]. Other presenting symptoms in this study included fever, pyuria, urinary frequency, hematuria, obstructive uropathy, and renal impairment (Table ??). Nevertheless, all symptoms detailed in Table ?? are nonspecific and can also be present in various other illnesses such as urinary tract infections (UTIs), cancer, and urolithiasis. Therefore, a high index of suspicion is necessary for the early detection of a UGTB. Physicians must remember GUTB in all instances of UTI, urogenital cancer, and stone disease, as it can imitate these illnesses and occasionally coexist with them. Therefore, UGTB should be suspected in patients from TB-endemic areas or with a history of pulmonary tuberculosis who present with

unexplained urogenital symptoms. UGTB should also be considered in cases of recurrent UTIs with sterile pyuria that do not respond to standard antibiotic therapy.

Complete blood counts, C-reactive protein (CRP), and renal function tests are nonspecific for UGTB, however, these tests are useful adjuncts to more confirmatory testing and may be useful in assessing disease response to treatment.[12] QuantiFERON-TB Gold in-tube assay with the peripheral blood is reported to have a sensitivity of 52.6% in detecting UGTB.[16] In our study, QuantiFERON-TB Gold in-Tube assay was performed 95 times. It was positive in 67(70.5%) cases, while it was inconclusive in 4(4.2%) cases and negative in 24(25.3%).

The gold-standard test in diagnosing GUTB or TB, in general, involves the demonstration of the causative M. tuberculosis in clinical samples.[12] In addition, histopathological identification of caseating granuloma in urogenital biopsy tissue and the presence of acid-fast bacilli are hallmarks of UGTB.[17] In most studies, the diagnosis of UGTB was made by direct identification of bacilli or culture growth and/or histopathological identification of a caseating granuloma in a urogenital specimen.[8,10,14,15,18] In our study, the diagnosis of UGTB was made in 32.1% (n = 34) of patients by direct bacilli identification or culture growth and in 51.9% (n = 55) of patients by histopathology.

In 10%-33% of patients with UGTB, diagnosis is presumptive and based on a combination of strong clinical, laboratory, and radiographic evidence, without microbiological or histological confirmation plus clinical improvement after empirical antituberculosis therapy.[8,10,18] In the current study, a presumptive diagnosis was established in 16.0%(n=17) of patients, which falls within the above-mentioned range.

The management of GUTB requires input from various specialists such as an Infectious diseases specialist, a urologist for urinary tract complications, a gynecologist for female reproductive organ issues, a radiologist for efficient image interpretation or intervention, and an infectious diseases pharmacist.

Drug treatment of UGTB should be started after microbiological or histological diagnosis and even before confirmation of the diagnosis when clinical, laboratory, and radiological data justify a preliminary diagnosis,[4,8,19] The most acceptable treatment plan is to start a four-drug regimen, which includes isoniazid, rifampin, pyrazinamide, and ethambutol or streptomycin. In our study, all patients received anti-tuberculous therapy. The majority of patients (93.4%) were prescribed a 4-drug antituberculosis treatment, consisting of Isoniazid, Rifampicin, Ethambutol, and Pyrazinamide, whereas a small percentage (6.6%) received second-line therapy such as linezolid, moxifloxacin, amikacin, and levofloxacin. Although the optimal treatment duration has not been defined, drug-susceptible UGTB can usually be managed with regimens suitable for pulmonary tuberculosis as discussed elsewhere.[19] In our study, the mean of treatment duration was 3.043.69(1-12 months). The variation in the duration is attributable to the fact that some patients left Qatar before treatment completion.

Almost all studies in the literature report surgical interventions in patients with UGTB, with the percentage of patients undergoing surgery varying between 8 and 95% depending on the time of diagnosis.[9,10,18] The later the diagnosis, the greater the need for surgery due to organ damage. As a rule, surgery is done after at least 3-4 months of optimal treatment with antituberculosis medications but sometimes an emergency procedure like stenting and percutaneous nephrostomy may be needed.[9] In our series, surgical intervention was reported in 73(68.9%) cases, which falls within the global range.

4.1. Limitations of study

The main limitation of this study is its retrospective design. All patient data are limited to those recorded by the treating physician. In addition, most patients were lost to follow-up after completion of anti-tuberculosis therapy, so no information on long-term outcomes and relapses was available.

5. Conclusion

UGTB accounted for 0.4 percent of all TB cases and an incidence of 0.7 new UGTB cases per 100,000 population in Qatar. The diagnosis of UGTB is generally delayed due to vague clinical features. Awareness of UGTB is essential for physicians to suspect this disease in patients with unexplained urogenital symptoms, especially in patients from TB-endemic areas or with a history of pulmonary tuberculosis. The diagnosis of UGTB can be made by direct identification of bacilli or culture growth and/or histopathological identification of a caseating granuloma in a urogenital specimen. Drug treatment of UGTB should preferably be initiated with a 4-drug regimen after microbiological or histological diagnosis. Empirical antituberculosis therapy should be initiated when clinical, laboratory, and radiological data justify a preliminary diagnosis. Although chemotherapy is the mainstay of treatment, surgery is often required in the treatment of GUTB. We recommend conducting a prospective population-based study to overcome the limitations identified in our study.

6. Authors' Contribution

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, data analysis, and interpretation, or all these areas. All authors took part in drafting, revising, or critically reviewing the article and gave

final approval of the version to be published.

7. Source of Funding

None.

8. Conflict of Interest

None.

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