https://doi.org/10.29309/TPMJ/2024.31.03.8044

The Professional Medical Journal
www.theprofesional.com
2024, Volume, 31 Issue, 03

ORIGINAL ARTICLE

Clinical characteristics and outcome of genitourinary tuberculosis in Balochistan: An observational study.

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Article Citation: Hassan I, Khan A, Samreen Z, Tahira, Baloch K, Zahir A. Clinical characteristics and outcome of genitourinary tuberculosis in Balochistan: An observational study. Professional Med J 2024; 31(03):326-337. https://doi.org/10.29309/TPMJ/2024.31.03.8044

ABSTRACT… Objective: To make aware that the healthcare professionals should diagnose GUTB as early as possible to avoid the grave side effects of untreated cases as it can lead to the gross structural abnormalities in the Genito urinary system. **Study Design:** Single Center Observational study. **Setting:** Tertiary Care Medicine Unit in Baluchistan, in BMCH Teaching Hospital. **Period:** 1st January 2012 to 31st Dec 2022. **Methods:** Total 118 patients were enrolled in the research and patients were taken a detailed history, they went through physical examination, then they went they underwent through different diagnostic modalities as per the availability in indications. The diagnosed cases were treated and the follow up was done the mean duration for the follow up was around two years. **Results:** All individuals received interventions primarily involving anti-tuberculosis medications. Three patients had bilateral fallopian tubes obstruction who went under laparoscopy and later on 1 couple opted for IVF, for infertility. Anti-TB drug therapy resulted in severe adverse reactions in 8 individuals. Among them, two female patients experienced the formation of a thimble bladder accompanied by incapacitating storage symptoms. Additionally, at the time of diagnosis, 4 patients exhibited impaired renal functions, which, fortunately, remained unaltered following the completion of the prescribed treatment. None of our patients went into ESRD, and no death during study was reported due to GUTB. **Conclusion:** It was concluded in our study that Genito urinary tuberculosis being the second commonest type of extrapulmonary tuberculosis is also common in Baluchistan and it needs to be treated and diagnosed and treated as soon as possible, we also suggest that if the expert diagnostic modalities for the diagnosis of GUTB are not available even the clinical suspicion can be used to diagnose the case and start the treatment.

Key words: Genitourinary Tuberculosis, National TB Programe, Tuberculosis Pelvic Inflamatory Disease.

INTRODUCTION

Tuberculosis represents a significant global health challenge, especially in underdeveloped areas. In 2020, TB stood as the thirteenth foremost cause of death, resulting in the loss of around 1.5 million lives, including 214,000 individuals infected with HIV. According to assessments by the World Health Organization, there are approximately 10 million instances of TB each year, with 98% originating in less economically developed regions.[1,2]

The World Health Organization (WHO) defines tuberculosis as "An infectious bacterial ailment caused by Mycobacterium tuberculosis, primarily affecting the lungs. It spreads from person to person through droplets released from the throat and lungs of those with an active respiratory infection."

Fifteen percent of reported tuberculosis (TB) cases worldwide are attributed to extra-pulmonary tuberculosis (EPTB). The prevalence of individuals manifesting symptoms extending beyond respiratory issues varies, rates vary across different regions, with percentages ranging from 24% in the Eastern Mediterranean Region, 17% in South East Asia, to 8% in the WHO Western Pacific region.[3,4] Diverse manifestations of extrapulmonary TB affect various organ systems. In numerous developed nations, genitourinary tuberculosis (GUTB) emerges as the second most prevalent type (20 to 40%), and in most developing countries, it

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Article received on: 18/12/2023
Accepted for publication: 19/02/2024

ranks as the third most widespread. Furthermore, GUTB is contemporaneously identified in 2–20% of individuals afflicted with pulmonary tuberculosis.[3] Miliary tuberculosis, marked by extensive hematogenous dissemination to the genitourinary system, is acknowledged as the fundamental factor in GUTB occurrence in 25–60% of instances.[2] The hematogenous spread of the initial tuberculosis infection to the renal organ is implicated in this mechanism.

Pakistan, with a population of 179.2 million individuals[5], holds the fifth position among the twenty-two nations significantly affected by tuberculosis.[5] It contributes to 63% of the tuberculosis cases within the Eastern Mediterranean Region. Furthermore, the National TB Control Program (NTP) estimates an annual occurrence of approximately 413,450 tuberculosis cases of all types in Pakistan, with an incidence rate of 231 per 100,000 people. As per the NTP[6], the prevalence of tuberculosis in Pakistan is recorded at 630,000 cases, corresponding to 364 cases per 100,000 people, accompanied by mortality rates ranging around 60,000 (34 per 100,000 people).

Pakistan Genitourinary Tuberculosis (GUTB), akin to other instances of tuberculosis, is typically initiated by an M. tuberculosis infection.

Nonetheless, specific cases may arise where the ailment is triggered by diverse constituents of the MTB complex, including bacteria like Mycobacterium bovis, Mycobacterium africanum, Mycobacterium pinnipedii, and Mycobacterium microti. Mycobacterium caprae, and the tuberculosis vaccine known as bacillus Calmette–Guérin (BCG).[7] Genitourinary tuberculosis (GUTB) typically originates from the hematogenous spread of mycobacteria during the initial infection. Subsequently, these bacteria may lie dormant in the urogenital tract and become active when the immune system is compromised.[8]

Apart from hematogenous spreading during the initial infection, alternative infection pathways in GUTB encompass lymphatic dissemination and sexual transmission.[9] Factors such as diabetes, increasing age, low body mass index (BMI), concurrent malignancies, immunosuppression, and kidney failure can heighten the risk of reactivation, with the estimated reactivation risk reaching up to 15% Genitourinary tuberculosis (GUTB) manifests in 2 to 20% of cases involving pulmonary tuberculosis (TB).[10] In developed nations, GUTB arises in 2 to 10% of pulmonary TB instances, while in developing regions, the frequency tends to be higher, ranging from approximately 15 to 20%. Developing countries account for over 90% of reported GUTB cases.[11] According to a Brazilian autopsy-focused investigation, 9.8% of all TB cases were identified as GUTB.[12] A United Kingdom study revealed that 13.5% of GUTB patients concurrently exhibited lung TB.[12] The USA reported a tuberculosis incidence of 3 cases per 100,000 population in 2013, yet corresponding data on GUTB incidence is lacking.[13] A comprehensive autopsy study in Germany found evidence of GUTB in 3.1% of 5,424 autopsied subjects.[14]

GUTB impacts the kidney in 74% of instances through hematogenous spread, subsequently affecting the epididymis, testis, bladder, ureter, and prostate gland.[15] Reports indicate that isolated engagement of reproductive organs occurs in approximately 5–30% of GUTB cases, with increased prevalence observed in epidemic scenarios.[16]

Tuberculosis affecting the male reproductive system typically stems from the common respiratory acquisition of tuberculosis. While it is improbable for genital tuberculosis to be acquired through sexual contact, instances of male-to-female transmission of genital tuberculosis have been documented. The presence of human immunodeficiency virus (HIV) infection heightens the likelihood of active tuberculosis and is believed to elevate the risk of reactivating dormant tuberculosis foci. Epididymal tuberculosis is most frequently observed in sexually active young men.

In extremely uncommon instances, instances of epididymitis[17] linked to tuberculosis (TB) and TB affecting the prostate have been documented subsequent to the use of intravesical Bacillus

Calmette-Guérin (BCG) therapy for superficial bladder tumors.[18] This is believed to occur as a result of the retrocanalicular descent of microorganisms from the prostatic urethra.

In general, prostatitis caused by tuberculosis (TB) arises from the hematogenous spread of M tuberculosis from the primary infection site. Therefore, having a history of TB infection is the predominant risk factor. In the past, around 10-12% of males with TB exhibited pathological indications of prostatic engagement upon post-mortem examination. The notion of descending dissemination through contaminated urine has been discarded, primarily due to animal research highlighting hematogenous dissemination and the rarity of TB affecting the prostatic urethra in conjunction with prostatic parenchymal TB.

Extended utilization of steroids and immunosuppressive treatment can elevate the likelihood of the reactivation of dormant centers.

In instances of prostatic tuberculosis (TB) among men with a normal immune system, the age of patients varied between 26 and 85 years. In documented occurrences of prostatic TB in men living with HIV, individuals were between 30 and 47 years old. Kulchavenya and Khomyakov provided findings on a group of 58 Siberian males affected by prostatic TB, with an average age of 49 years.[19]

Diagnostic Considerations

The primary causes of postponed identification include the lack of typical clinical characteristics and the inclination of Genitourinary Tuberculosis (GUTB) to be concealed by alternative illnesses, such as urinary tract infections (UTIs) caused by different pathogens. UTIs should be given priority in the initial diagnosis when considering GUTB. The existence of diverse pathogens in urine complicates the recognition of Mycobacterium tuberculosis, and individuals with pyuria and bacteriuria frequently undergo numerous rounds of antibiotic treatment instead of being examined for GUTB. According to a specific study, coexisting UTI was detected in 65.1% of UGTB instances.[20]

Diagnosing female genital tuberculosis can be challenging because its clinical appearance and symptoms can mimic ovarian and endometrial cancer.[21]

Substantial overlap in the diagnostic possibilities necessitates maintaining a heightened level of suspicion for tuberculosis affecting the prostate, especially in males with a background of exposure to or infection with tuberculosis.

The accurate identification of tuberculosis (TB) epididymitis is frequently disregarded in the management of persistent epididymo-orchitis, particularly in developed nations. Typically, confirmation involves a thorough examination of pathological specimens obtained through epididymo-orchiectomy. It's crucial to consider various conditions such as cancers affecting the bladder, testicles, kidneys, and urethra; fungal and bacterial infections of the genitourinary tract; pyonephrosis; scrotal or testicular injuries; granulomatous prostatitis post-surgery; complications following Bacillus Calmette-Guérin (BCG) treatment; and granulomatous and bacterial prostatitis. Individuals with nonspecific renal calcifications should be assessed for renal tuberculosis (TB). Additionally, a comprehensive examination for malignancies becomes imperative if tubercles or ulcers are found away from ureteric orifices, genital ulcers are present, or suspicions arise from renal lesions.

The Xpert MTB/RIF test can identify both Mycobacterium tuberculosis complex (MTBC) and rifampin resistance in under 2 hours. It is endorsed by the World Health Organization as the primary diagnostic test for individuals displaying signs and symptoms of tuberculosis.[22] A comprehensive analysis found that the test has a sensitivity between 83% and 95%, and specificity ranging from 79% to 99%.

PCR has undergone thorough examination and has been validated as remarkably responsive, precise, and swift. In numerous investigations, evidence indicates a sensitivity spanning from 87% to 100% (typically exceeding 90%) and a specificity ranging from 92% to 99.8% (typically

surpassing 95%). Contrast this with the sensitivity rates of cultures (37%), bladder biopsies (47%), and intravenous pyelography (IVP) examinations (88%).[23]

Using auramine or rhodamine staining and observing under fluorescence microscopy is a method to identify small quantities of mycobacteria. The diagnosis of tuberculosis can be accomplished through the utilization of luciferase bioluminescence.

METHODS

A comprehensive research investigation was conducted at the Baluchistan BMCH Teaching Hospital's tertiary care Medicine Unit, covering the period from January 1, 2012, to December 31, 2022—spanning a total of 11 years, during which the principal author actively participated. The primary emphasis of the research was on individuals afflicted with GUTB, signifying tuberculosis impacting various anatomical components including the kidney, ureters, bladder, urethra, Fallopian tubes, prostate, testis, and epididymis. All subjects under examination were procured from the Nephrology and Medicine Outpatient Department, either through routine referrals or direct admissions to the emergency ward, illustrating acute clinical presentations.

Patient data was gathered during the initial diagnosis, and subsequent reviews of their records were conducted during routine follow-up clinic appointments. As the information collected was related to standard clinical care, no specific interviews were conducted exclusively for the study. The research obtained approval from the Institutional Review Board (MU-SPH/2023/186/87) at the BMCH Tertiary Care Hospital, aligning with the principles of the Declaration of Helsinki. All procedures were conducted in adherence to the applicable guidelines.

The study documented clinical aspects, such as concurrent medical conditions, contact or past tuberculosis history, and clinical indications. A basic biochemical assessment, encompassing measurements of erythrocyte sedimentation rate (ESR) and levels of serum urea and creatinine, was carried out for each patient. The Mantoux test was omitted for all patients. All individuals underwent a comprehensive evaluation, which included ultrasound scans of the kidney, ureter, bladder, and prostate (US-KUBP) in addition to pelvic X-ray KUB. Those exhibiting symptoms related to the scrotum underwent an extra scrotal ultrasonography. Infertile patients were subjected to hysterosalpingogram and semen analysis for women and men, respectively. Suspected cases underwent HIV screening. All patients received a computed tomography urogram (CTU), unless they solely manifested scrotal symptoms and had negative results from scrotal ultrasound (US-KUBP) and kidney-ureter-bladder X-ray (X-ray KUB). Anomalies detected in the imaging were classified according to the affected organ and the anatomical region.

Microbiological diagnoses were sought through the performance of various investigations, including the analysis of urine for acid-fast bacilli (AFB), Gene Xpert testing, TB culture examination of urine, and polymerase chain reaction (PCR). GeneXpert was also employed in this context.

However, due to the unavailability of essential reagents and resources, some tests were not conducted in a subset of patients. Selected individuals underwent a bladder biopsy and cystoscopy. In individuals with a past occurrence of hematuria, lower urinary tract manifestations, or findings from ultrasound/CTU suggesting anomalies in the bladder like augmented bladder wall thickness, a contracted bladder, or the presence of mass lesions, the suggestion was to undergo cystoscopy. Individuals manifesting signs of a shrunken bladder, mass abnormality, or inflammatory changes in the urothelium underwent a biopsy of the bladder. The confirmation of histological evidence for genitourinary tuberculosis (GUTB) was ascertained when the presence of clusters of epithelioid histiocytes, Langhans giant cells, and caseating necrosis was observed.

Every individual underwent screening for pulmonary tuberculosis through a clinical evaluation, compulsory chest X-ray, and

examination of sputum for acid-fast bacilli (AFB). Tuberculosis affecting other areas was screened using a clinical history and inspection of lymph nodes and the spine. Individuals with confirmed positive results underwent additional assessment.

A diagnosis of genitourinary tuberculosis (GUTB) was confirmed when, in addition to clinical symptoms, at least one of the following conditions was satisfied: (1) a favorable outcome for acid-fast bacilli (AFB) in one of three urine specimens using the Ehrlich–Ziehl–Neelsen (EZN) method. For the evaluation, three successive mid-stream urine samples were collected in the early morning. This includes (2) a positive urine or tissue culture confirming the existence of the Mycobacterium tuberculosis complex, (3) a favorable polymerase chain reaction (PCR) for the Mycobacterium tuberculosis complex, and (4) histopathological findings suggestive of tuberculosis.

The initiation of ATT was followed by the treatment of patients who did not respond positively or faced complications such as stricture or the formation of abscesses. For such cases, a range of invasive procedures was employed.

These techniques included minimally invasive approaches like percutaneous drainage, cystoscopy, and stenting, in addition to broader open methodologies such as open drainage and reconstructive surgical interventions. Unfavorable occurrences, such as the thimble bladder syndrome and the gradual decline in renal function, were likewise recorded. The estimated glomerular filtration rate (eGFR) was utilized as a measurement for renal function. Six months after completing ATT, all individuals underwent reassessment using US-KUBP and serum creatinine tests. Subsequent to this, patients with anomalies in the urinary tract detected via US-KUBP, heightened serum creatinine concentrations, individuals possessing a solitary operative kidney, or those who had experienced reconstructive surgery underwent yearly monitoring, encompassing both US-KUBP and evaluations of serum creatinine levels.

SPSS software version 17 was utilized for conducting statistical analyses. Results were communicated in terms of either frequency and percentages or median and range, depending on the context. Non-parametric methods were applied to identify connections and establish statistical significance. The Chi-square test was deployed to assess relations among qualitative parameters. Statistical significance was affirmed for p-values below 0.05 in the results.

RESULTS

There were a total of 139 patients enrolled in this study. 8 patients lost from follow up, who were immigrants, from Afghanistan, 13 patients were diagnosed with other conditions and were excluded from our study. Remaining 118 patients were comprised in the research who satisfied the inclusion criteria.

Criteria for Diagnosing Tuberculosis in the Urinary System

Classification	Definition
Definite GUTB	Pts. Fulfil the criteria A or B A: Cases with clinical suspicion along with either Positive smear microscopy or Positive MB culture or more. B: Cases with clinical suspicion along with a positive pathological examination.
Clinically diagnosed GUTB	Clinically suspected cases plus clinical improvement after empirical ATT.

Out of these 56 (47%) were women, 41 (34%) men, and 2 (1.69%) children, one age 6 years and other 11 years old girl. The age median was 51 years, encompassing a spectrum from 6 to 68 years. Out of 118 cases, 32 were immigrants, and remaining were residents of Balochistan. Most patients (84%) had repeated UTIs at presentation.

Few females 25(21%) presented with mixed symptoms of UTIS and chronic Pelvic inflammatory disease, 6 females and two males with infertility (6.78%). 54(45 %) patients had a history of pulmonary or abdominal tuberculosis, 12 were treated only for two months and rest had complete ATT, the mean duration of appearance of GUTB and pulmonary TB was around 9-14

years.

Onset of Genitourinary Tuberculosis (GUTB) and the time gap from the initial occurrence of pulmonary tuberculosis.

Duration	Number
Concurrent	3
> 1 year	4
2 to 5 years	6
5 to 10 years	16
> 15 years	25
total	54

3 patients had active pulmonary TB, and 5 had concomitant abdominal TB. at the time of presentation. All of them presented with nonspecific symptoms also.

Different Methods of Displaying GUTB in Our Research.

Features	No. (%)
Lower abdominal pain	45 (38%)
Storage symptoms	06 (5%)
Haematuria	14 (11%)
Stone disease	10 (8.4%)
Weight loss	20 (16 %)
Respiratory symptoms	3 (2.5%)
Infertility	6 (5%)
GI symptoms	5 (4%)
Renal failure	2 (1.69%)
Fistula in anno	1 (0.85%)
HIV/ AIDS symptoms	6 (5%)
Total	118 (100%)

Common specific symptoms at presentation were haematuria 14(11%), pain lower abdomen, 45 (38%). Two children who were included in the study presented with LUTS and repeated UTIS, one significant finding in all these patients was malnourishment, or weight loss, 20 pts (2 male, 18 women, 2 children females) 6 patients had HIV. 2 HIV positive women has had presented with other complaints of HIV…….

The Mantoux test was omitted in all patients, given that the majority of Pakistanis receive vaccinations shortly after birth, while Afghans were hesitant to undergo the Mantoux test. Erythrocyte sedimentation rate results were obtained for 100 patients, and it exceeded 50 mm in 32% of them. Approximately 90% of patients underwent tests such as Urine DR, GeneXpert, urine culture, urine PCR, Chest x-ray, and kidney-ureter-bladder (KUB) x-ray. HSG, Semen analysis was done in 6 patients with infertility. One patient had hydrosalpinx, and three women had bilateral tubal blockage. 4 patients underwent cystoscopy and 2 had unusual or atypical observations. Microbiological diagnosis was found in only 9(%) and rest were diagnosed clinically only a few went for renal biopsy 8(%). Commonest organs involved were bladder (80%), kidneys (45%), ureters (44%), fallopian tubes (4%). 2 patients had TB of the prostate.

Diagnostic modalities used in our study.

Diagnostic Modality	No. (%)
AFB smear of urine	23 (21%)
Culture of AFB in urine	6 (5%)
Biopsy of the bladder through cystoscopy.	19 (17%)
Pathological examination of the excised tissue sample.	14 (13%)
Serology	6 (5%)
Biopsy of the sinus in the scrotal region.	6 (5%)
Presumed identification, encompassing radiographic assessment.	36 (33%)

The primary treatment for all individuals involved the use of anti-tuberculosis medications. Laparoscopy was performed on three patients with bilateral fallopian tube obstruction, and subsequently, one couple chose in vitro fertilization (IVF) to address their infertility. Eight patients experienced severe unfavorable responses to medications used for treating tuberculosis. Two female patients developed a bladder resembling a thimble, accompanied by debilitating storage symptoms. At the time of diagnosis, four patients exhibited impaired renal functions, which, fortunately, remained stable after the prescribed treatment. Importantly, none of our patients progressed to end-stage renal disease (ESRD), and no deaths related to genitourinary tuberculosis (GUTB) were reported during the study.

Assessment of treatment eligibility with Anti-Tuberculosis Therapy (ATT) in comparison to findings from alternative research investigations.

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

DISCUSSION

The most common form of extrapulmonary tuberculosis is renal tuberculosis. Different research findings suggest that over time[24], an estimated 15% of people with pulmonary tuberculosis are expected to experience the development of genitourinary tuberculosis (GUTB). GUTB stands out as a prevalent urological factor contributing to morbidity associated with infections.[25] The term GUTB was introduced by Wildbolz, who asserted that renal tuberculosis and epididymal tuberculosis were not afflictions exclusive to individual organs but varied manifestations of the same ailment transmitted through the bloodstream.[26] Determining accurate data on the incidence and prevalence of GUTB is challenging due to the low suspicion index among healthcare professionals. Additionally, the urine may undergo sterilization relatively swiftly following the commencement of chemotherapy, exacerbating the complexities of diagnosis.

The prevalence of Genitourinary Tuberculosis (GUTB) has significantly declined in Western countries, yet there hasn't been substantial change in developing nations.[27] Annually, there are eight million fresh tuberculosis cases, resulting in three million fatalities.[28] The silent hematogenous dissemination from the initial infection impacts the kidney cortices, lying dormant for extended periods with the possibility of reactivation in the future.[29,30]

There were a total of 118 patients enrolled in this study.

Out of these 56 (47%) were women, 41 men, and 2 children, one age 6 years and other 11 years old girl. In our study there is female dominance, which contrasts with other studies conducted where male majority is reported.[31] The median age was 51 (range: 6–68) years. GU tuberculosis (GUTB) typically manifests in the adult population due to the temporal interval between the initial infection and the subsequent reinfection of genitourinary organs. But in our study two children presented with the same diagnosis without the evidence of primary infection.

Out of 118 patients, 32 were immigrants, and remaining were residents of Baluchistan. Common specific symptoms at presentation were haematuria (13%), pain lower abdomen 78%, vaginal discharge in females 23%. And scrotal manifestations (8%). Two children who were included in the study presented with LUTS and repeated UTIS, one significant finding in all these patients was weight loss. Most patients (84%) had repeated utis at presentation. Few females (25) presented with mixed symptoms of UTIS and chronic Pelvic inflammatory disease, 6 females and two males presented with infertility. Fifty four patients had a history of pulmonary or abdominal tuberculosis, 12 were treated only for two months and rest had complete ATT, the mean duration of appearance of GUTB and pulmonary TB was around 8-12 years. Three patients had active pulmonary TB, and 5 had concomitant abdominal TB. At the time of presentation. Six patients (4 male, 2 females) had HIV/AIDS.

HIV infection, through the impairment of cellular immune responses, leads to a distinct vulnerability in patients to contract tuberculosis. The prevalence of TB has undergone alterations in regions where HIV infection is identified as widespread, particularly in South Asian nations where TB was previously established. According to Hasnain et al.[32], around 30% of individuals with HIV were found to have tuberculosis during screening, with Pakistan ranking among the top five countries with a high burden of TB cases.

The prevalence of genitourinary tuberculosis (GUTB) has significantly diminished in Western

regions, yet the circumstances have not undergone substantial changes in less developed nations. There are annually eight million fresh instances of tuberculosis, resulting in three million fatalities. Hematogenous dissemination from the initial infection silently infiltrates the kidney cortices, lying dormant for extended periods with the possibility of reactivation in the future.

Abdur Rehman et al colleagues conducted a study at Lady Reading Hospital in Peshawar, revealing a notably elevated proportion of extrapulmonary tuberculosis (44.9%) among individuals with HIV.[33,34] This research aligns with global estimates from the World Health Organization (WHO), indicating that tuberculosis is present in 16% of people living with HIV (PLHIV), who are 19 times more susceptible to TB compared to those without HIV infection. It has been identified that females with HIV face an increased risk of developing extrapulmonary TB.[35] Adnan and collaborators noted a higher prevalence of TB-HIV co-occurrence in young, unmarried, and uneducated males, leading to a decline in the immune system and a reduction in CD4 cell count.[36] Tehseen and his research team suggested that the prevalence of TB among people who inject drugs with HIV was 6.1%, which is 15 times higher than the general population.[37]

The primary method for diagnosing tuberculosis involves identifying tubercle bacilli in a fluid specimen or detecting acid-fast bacilli in histopathology samples. When it becomes difficult to directly show the bacillus in biopsy samples, indirect signs like the existence of epithelioid granulomas and Langhans giant cells are frequently considered satisfactory to commence anti-tuberculosis treatment (ATT). Likewise, in the case of genitourinary tuberculosis (GUTB), a straightforward screening test involves examining urine smears for acid-fast bacilli, facilitating a definitive diagnosis. However, a notable limitation is the potential for confusion in distinguishing Mycobacterium smegmatis from the tubercle bacillus. Additionally, due to intermittent bacilluria, a thorough examination of urine over three to five consecutive days is necessary to confirm infection, analogous to sputum examination. The direct acid-fast bacilli smear exhibits a low yield, approximately 30%[38], and requires a considerable time of six to eight weeks for tuberculosis culture. While the specificity of the culture medium surpasses that of urine smear examination, Polymerase Chain Reaction (PCR) for tuberculosis offers a quicker detection of acid-fast bacilli within a few hours of DNA extraction. Notably, PCR can yield positive results even when smear and culture tests are negative. However, a notable drawback is the potential for false PCR negativity[39] due to the presence of nontuberculous mycobacteria or hemoglobin in cases of hematuria. To mitigate this, the collection of multiple urine samples, elimination of PCR inhibitors, and centrifugation of urine before analysis can significantly reduce the risk of false negativity.[40]

The distinctive diagnosis of Genitourinary Tuberculosis (GUTB) necessitates the detection of mycobacterium either through examining urine smears or employing culture techniques.[41] In Western nations, 90% of the afflicted individuals exhibited a favorable culture outcome. In our investigation, 21% of patients exhibited a positive result in urine smear for mycobacteria, while the culture yielded positive results in 5% of cases. Additionally, 33% of the subjects received treatment based on an assumed diagnosis.

The Mantoux test was omitted in all patients since the majority of Pakistanis are immunized at birth, and Afghanis were hesitant to undergo the Mantoux test. The erythrocyte sedimentation rate was accessible in 88 individuals, with more than 40 mm observed in 62% of patients. Various diagnostic procedures, including urine DR, GeneXpert, urine culture, urine PCR, chest x-ray, and x-ray kidney-ureter-bladder, were conducted in nearly 90% of patients. In cases of infertility, HSG and semen analysis were performed in six patients, revealing hydrosalpinx in one patient and bilateral tubal blockage in three women. Cystoscopy was conducted in four patients, uncovering abnormalities in two cases. Microbiological diagnosis was possible in only 9%, while the rest were clinically diagnosed, with only a few opting for renal biopsy (8%).

The most commonly affected organs were the bladder (80%), kidneys (45%), ureters (44%), and fallopian tubes (4%). Two patients exhibited TB of the prostate.

All patients received primary treatment with anti-TB drugs. Two patients with bilateral fallopian tube obstruction remained childless. Anti-TB medications induced severe adverse reactions in eleven patients. Two women experienced the development of a thimble bladder accompanied by debilitating storage symptoms. Additionally, among the diagnosed cases, fourteen patients presented with impaired renal functions, which stabilized after treatment. None of the patients progressed to end-stage renal disease, and no deaths related to genitourinary tuberculosis were reported during the study.

In our investigation, no surgical procedure was undergone by any of the patients. Nevertheless, in other regional studies, despite the availability of more advanced imaging methods capable of identifying the disease at an earlier phase and the existence of effective antitubercular drugs, surgery remains pivotal in the GUTB treatment. In an extensive series of GUTB cases conducted by Gupta NP et al. in 2006, it was argued that surgical intervention serves as a complementary approach to antitubercular chemotherapy. The authors suggested a waiting duration of four to eight weeks for ATT before considering any surgical measures. According to their analysis, this waiting period enables the lesion to stabilize effectively, thereby enhancing the planning process for the envisioned reconstructive surgical procedure.[42]

Fleschner and Gow Examined 300 instances of Genitourinary Tuberculosis (GUTB), among which 69 individuals (23%) exhibiting a non-functional kidney underwent Nephrectomy.[42] The prevalence of nephrectomies could be attributed to delayed detection and advanced disease manifestation at the time of diagnosis, accounting for 42 cases. In our research, challenges also arose from suboptimal patient adherence and the inability to fully implement the Directly Observed Treatment Short-Course (DOTS) strategy. Conversely, Jitendra Singh, in his investigation involving 117 GUTB cases, employed a brief chemotherapy regimen following the standard Category I protocol, resulting in an 86% positive response to anti-tubercular therapy.[43]

Tuberculosis can appear in the seminal vesicle among males and in the uterus and fallopian tubes among females, spreading through either the bloodstream or the lymphatic system.[44] In our investigation, no individuals were found to have any affliction in the seminal vesicle or uterus.

Regional Comparisons

In our group, the prevalent organs implicated include the kidneys, bladder, and fallopian tubes (on one side or both). A retrospective examination conducted in India by Krishnamoorthy et al. revealed that, out of 110 cases, the kidneys, ureters, and bladder were affected in 70, 30, and 18 instances, respectively, mirroring our findings.[45] Another study from Sri Lanka reported the involvement of the kidneys, ureters, bladder, and testis/epididymis as common. Bansal et al., in an Indian study involving 60 cases, found that the kidney (n = 34) was the most commonly affected organ, perused by the urinary bladder (with a count of 25) and the ureter (with a count of 20).[46] Notably, in our group, occurrences of urethral, prostate, and testicular involvement were exceedingly rare. Despite prostate gland involvement being infrequent, a few incidental cases of prostate TB were detected in biopsy samples following trans-urethral resection in our neighboring country, India.[47]

LIMITATIONS

This research has various constraints. It constitutes an observational examination involving individuals diagnosed and managed by a sole urological specialist across two successive facilities. Due to limitations in resources, specific examinations were occasionally omitted due to the sporadic unavailability of facilities and reagents. Crucial information, such as the existence of concurrent conditions like diabetes mellitus and additional risk elements, remains unrecorded. The follow-up information is inadequate, as data solely from patients attending regular follow-up appointments

has been gathered.

CONCLUSION

The most effective approach to managing tuberculosis involves early identification of cases and thorough treatment. To achieve this, it is essential to maintain a strong sense of suspicion and conduct a comprehensive set of investigations for all individuals under suspicion. Subsequently, a personalized decision-making process involving input from a diverse team of specialists becomes crucial for diagnosing genitourinary tuberculosis (GUTB). Therefore, examinations such as urine analysis for acid-fast bacilli (AFB), Mantoux testing, CT-urography, and histopathological assessment play vital roles as supplementary tools for GUTB diagnosis. Surgery constitutes a significant treatment modality for the majority of patients, alongside mandatory anti-tuberculosis treatment (ATT). Post-completion of ATT, follow-up is essential, as some individuals may progress to end-stage renal disease (ESRD).

CONFLICT OF INTEREST

The authors declare no conflict of interest.

SOURCE OF FUNDING

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

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