

## A Review of Urogenital Tuberculosis in Nigeria: Epidemiology, Pathogenesis, Clinical Manifestation, Diagnosis, Treatment Strategies, Risk Factors, and Prevention Control Measures

Garba D. E.<sup>1,2\*</sup> Dibua U. M. E.<sup>1</sup> Oka C. U.<sup>1</sup> Ozoadibe Y. O.<sup>1</sup> Ajah M. I.<sup>1</sup> and Attah F.<sup>3</sup>

1. Department of Microbiology, Faculty of Biological Sciences, University of Nigeria, Nsukka, Enugu State, Nigeria.

2. Department of Microbiology, Faculty of Natural Sciences, Prince Abubakar Audu University, Anyigba, Kogi State, Nigeria.

3. Department of Microbiology, Confluence University of Science and Technology, Osara, Kogi State, Nigeria.

\* Corresponding author: [danisunville@gmail.com](mailto:danisunville@gmail.com)

**Abstract:** Urogenital tuberculosis (UGTB) is a significant public health concern in Nigeria, where tuberculosis (TB) is endemic. Despite its importance, UGTB remains a neglected and underdiagnosed condition, leading to delayed diagnosis, inadequate treatment, and poor health outcomes. This review aims to provide an overview of the epidemiology, pathogenesis, clinical manifestations, diagnosis, treatment strategies, risk factors, prevention and control measures of UGTB in Nigeria. A comprehensive literature search was conducted using Google Scholar, PubMed, Scopus, and Nigerian Journals Online by a combination of search terms related to UGTB. Studies published in English between 2000 and 2024 were included. The selected articles were vitally appraised using standardized forms to assess study quality. The qualitative data from each study was analyzed to identify underlying themes related to UGTB. Eight sources met the eligibility criteria and were included in the review. The review revealed that UGTB is a common extrapulmonary manifestation of TB in Nigeria, with a prevalence of 27% of all extrapulmonary tuberculosis cases. It further highlighted the epidemiological characteristics of UGTB in Nigeria, including the clinical features observed in affected patients. The importance of raising awareness, enhancing diagnostic capabilities, and improving treatment strategies to address the burden of UGTB in Nigeria was underscored. The review concluded that effectively managing the burden of UGTB in Nigeria necessitates a comprehensive approach involving healthcare providers, policymakers, and researchers. Additionally, the review recommended integrating UGTB diagnosis and treatment into existing TB control programs to ensure the disease is effectively managed and controlled.

Key word: Extrapulmonary tuberculosis, *Mycobacterium tuberculosis*, pathogenesis, tuberculosis, urogenital tuberculosis

### INTRODUCTION

Urogenital tuberculosis (UGTB), a type of extrapulmonary tuberculosis (EPTB) caused by *Mycobacterium tuberculosis* (Mtb), is a significant global health issue frequently associated with urinary tract infections globally (Tobin *et al.*, 2024). Though UGTB is less common than pulmonary tuberculosis, accurate and timely diagnosis remains vital for prompt treatment and patient welfare. Extrapulmonary tuberculosis is when tissues in various organs of the body become infected. This includes infections in the reproductive and urological tracts. Infection can occur by inhaling *Mycobacterium tuberculosis* containing aerosols or by ingesting dairy products contaminated by *Mycobacterium bovis* (Roddy *et al.*, 2024).

Urogenital tuberculosis predominantly affects the kidneys and urinary tract, resulting in non-specific symptoms such as abnormally increased urine frequency, persistent lower back pain, blood in urine, and recurrent urinary tract infections (Adhikari and Basnyat, 2018). The kidneys can be affected through the spread of bacteria in the blood, lymphatic system, or from the lungs or intestines after initial infection. Renal tuberculosis (TB) is often characterized by the formation of granulomas induced by Mtb and also by the formation of granulation tissue with caseous necrosis, which are commonly found near the glomeruli (Muneer *et al.*, 2019). Bladder disease can occur as a result of a kidney infection, with Mtb descending through urine, or through the spread of bacteria in the blood or lymphatic system. In low-

endemic countries, the resemblance of UGTB symptoms with routinely observed urological disorders often leads to misdiagnosis, prolonging the duration of patient suffering and increasing the risk of morbidity. Primarily, this disease affects adults in the age range of 20-40 years but can also occur in children and the elderly (Kulchavenya, 2014a).

In Nigeria, a country significantly burdened with TB, the prevalence of UGTB is noteworthy as it accounts for 27% of all EPTB cases (WHO, 2018). The National Tuberculosis and Leprosy Control Programme also estimates that UGTB comprises roughly 27% of EPTB cases in Nigeria (NTBLCP 2019). These numbers highlight that this endemic has potential grave consequences for Nigeria's public health and signifies the urgent need for consistent research and funding towards its eradication. Despite this significant proportion, the condition remains widely neglected, especially in low-endemic regions. Notably, this variation in recognition can be attributed to UGTB's unconventional clinical presentation, which can easily be mistaken for other urological ailments (Muneer *et al.*, 2019). It is primarily a secondary infection, originating from a primary site in the lungs but then branching off to the kidney via hematogenous spread. Despite advances in healthcare, UGTB remains a pressing issue in developing countries but is increasingly observed in developed nations as well (Kulchavenya, 2014a).

Urogenital tuberculosis is often challenging to diagnose due to its non-specific symptoms and the necessity for specific laboratory tests (Figueiredo and Lucon, 2008). The anatomical landscape of UGTB, presenting with largely nonspecific symptoms and commonly resulting in bacteriologically negative reports, makes its diagnosis a significant clinical challenge. The diagnosis process of UGTB is multi-faceted, incorporating several contemporary methods, including clinical history, urinalysis, imaging techniques, biopsy, and

bacteriological tests. Tools currently utilised include radiological imaging, histopathological examination, and examination of urine for Mtb (Katoch, 2004; Kapoor *et al.*, 2008; Kho and Chan, 2012). However, difficulties arise due to the intricacy of these procedures and their economic costs in resource-limited settings like Nigeria.

A medical history, elevated by the presence of risk factors such as exposure to tubercle bacilli, immunodeficient state, or prior episodes of pulmonary TB, often acts as the initial hint towards a possible diagnosis of UGTB. Further research into more cost-effective and rapid diagnostic tools is thereby an unmet need in Nigeria. Thus, it is essential to acquaint medical practitioners and healthcare workers with the peculiarities of UGTB to ensure accurate identification and appropriate treatment. As one of the prevalent health issues in Nigeria, UGTB presents unique challenges for healthcare practitioners, patients, and policymakers in the country. Further complications arise from multi-drug resistance TB, with repercussions on the management and prognosis of UGTB (WHO, 2021). This review explores the epidemiology and prevalence of UGTB in Nigeria, detailing the pathogenesis, clinical manifestation, diagnosis, treatment strategies, risk factors, and prevention control measures.

### **Epidemiology and Prevalence of UGTB in Nigeria**

Urogenital tuberculosis has become a significant public health challenge in Nigeria. The precise prevalence of UGTB is challenged by underdiagnosis and underreporting. A 2020 study by the World Health Organization (WHO) estimated that Nigeria ranks among the top ten countries representing 64% of the global gap in TB case findings (WHO, 2020). Last data specific to UGTB are tough to come by, which limits understanding and capability to tackle this issue most efficiently.

The UGTB's rise in Nigeria is influenced by several factors to include conditions endemic to the country, such as a high

prevalence of human immunodeficiency virus (HIV), which plays a significant role as the weakened immune systems allow Mtb to attack various systems including the urogenital system (Oladele *et al.*, 2020). Other factors include lower socioeconomic conditions and TB stigma, leading to late or no presentation for medical care.

Although UGTB remains a significant health issue in Nigeria, the paucity of data on its prevalence compounds the problem. To address this pandemic of UGTB in Nigeria, an integrated and robust effort is required. Establishing epidemiological surveillance mechanisms and strengthening laboratory diagnostic capacity is crucial. The importance of alliance between TB control and HIV programs cannot be overstated (WHO, 2016), and requiring considerable upgrade to overcome the destructive synergy of HIV and TB related infections in Nigeria. Furthermore, public health education campaigns targeting the stigma associated with TB could provide significant relief, encouraging individuals at risk to seek early treatment and improving the nation's chances of better UGTB control.

### **Pathogenesis of UGTB**

The etiological agent, Mtb, responsible for UGTB, typically enters the urogenital system through hematogenous dissemination from a primary lung infection (Muneer *et al.*, 2019; Kalam Azad *et al.*, 2022). Once in the genitourinary system, it begins to multiply, virtually undetectable initially due to the lack of robust host inflammatory response. As the volume of bacilli increases with time, consequently a granulomatous reaction occurs, resulting in the formation of tuberculous granuloma nests (Kulchavenya, 2013). This pathophysiological process can remain dormant for years, eventually reactivating to cause symptoms as and when the host's immune system is compromised. The lengthy asymptomatic period coupled with non-specific clinical presentation outlines the diagnostic challenge of UGTB (Houben and Dodd, 2016).

In the context of Nigeria, the pathogenesis is further complicated by numerous factors such as poor socio-economic conditions, the co-infection with HIV, and inadequate healthcare infrastructure. The HIV/AIDS pandemic fuels the TB epidemic, as the immune suppression it causes precipitates reactivation of latent infections, further contributing to the high prevalence of UGTB. In addition, the poor healthcare system and lack of diagnostic facilities in Nigeria significantly hinder early detection and efficient patient management of UGTB, thus amplifying the disease burden. The worrying statistics and the tangible impact of UGTB in Nigeria highlight the need for substantial interventions. These must incorporate robust research to enhance understanding of the pathogenesis, early detection strategies, and effective, patient-centred treatment protocols.

### **Clinical Manifestation of UGTB**

Initial infection of UGTB may remain latent for a prolonged duration, making early identification challenging (Muneer *et al.*, 2019). It often presents with a wide array of non-specific symptoms, frequently misdiagnosed due to its inconspicuous initial presentation.

UGTB represents an enduring health challenge in Nigeria, demanding a comprehensive analysis that will echo the knowledge of its occurrence and toll on public health in the country. It affects the urogenital system - kidneys, ureter, bladder, urethra, and reproductive organs (Merchant *et al.*, 2013). It implies that the Mtb leaves its usual pulmonary habitat to invade the genitourinary tract, producing array of symptoms that oftentimes perplex the medical professionals.

However, any part of the urogenital system can be impacted, the renal system is often the most susceptible. Subsequently, understanding the potential symptoms and pathology of this condition is notably crucial in clinical practices. Kulchavenya (2014b) stated that the first clinical manifestation of UGTB often presents in the form of sterile pyuria and non-specific urinary tract

symptoms. However, advanced cases may present with pronounced disseminated pyuria and haematuria, along with uncontrolled weight loss and dangerous hypertensive symptoms (Kulchavenya, 2014b).

Common urinary symptoms include dysuria, frequency and nocturia, which arise due to the inflammatory process incited by the pathogen within the urinary tract (Muneer *et al.*, 2019). As the disease progresses, haematuria and flank pain can manifest, which usually signpost the involvement of the renal pelvis or bladder (Muneer *et al.*, 2019). Regrettably, by the time these symptoms are apparent, irreversible damage may have already occurred, highlighting the importance of early detection. Figueiredo and Lucon (2008) opined that the clinical presentations vary greatly, which further convolutes the diagnostic process. Haematuria, dysuria, frequency, abdominal pain, and sterility are among the many, often misinterpreted symptoms of UGTB.

Infertility represents a considerable symptom of UGTB, particularly among women. Disruptions in menstrual cycles and pelvic pain are notable indications, instigated by tuberculous salpingitis and endometritis (Eastwood *et al.*, 2001). Men, however, can experience epididymo-orchitis, leading to testicular pain and potentially sterility (Yadav *et al.*, 2017).

Systemic symptoms such as fever, night sweats, lethargy, anorexia and weight loss are also prevalent, usually indicating the advance of the disease. Regrettably, these symptoms can be mistaken for other ailments and potentially delay definitive diagnosis and effective treatment (Eastwood *et al.*, 2001).

The evasive nature of UGTB is likewise reflected in radiographic presentations that are often misdiagnosed as bladder cancer or urolithiasis. Leveraging advanced diagnostic tools like Polymerase Chain Reaction (PCR) and bioscopy for bacterial culture has shown promising outcomes for a more precise diagnosis.

## Diagnosis of UGTB

The urogenital tuberculosis is less common than pulmonary tuberculosis, but accurate and timely diagnosis remains vital for prompt treatment and patient welfare. The classic diagnostic approach for UGTB has been reliant upon urine microscopy to identify acid-fast bacilli (AFB), coupled with mycobacterial culture, clinical symptoms, and imaging tests (Ghaleb *et al.*, 2013). Despite being a long-established method of diagnosis, there are limitations in sensitivity and specificity, with varied results in sample populations. Consequentially, current diagnosis methods are not always effective or accessible. The gold standards for diagnosing UGTB include urine culture, PCR, computer tomography (CT), ultrasounds, and intravenous urography (Tobin *et al.*, 2024). However, these tests are often expensive, invasive, and several are time-consuming. The methods also require hospital facilities and diagnostic expertise that may not be available or affordable for many Nigerians.

Imaging methods play an essential role in the diagnostic process of UGTB. Among the available imaging techniques, ultrasound and CT scans have become indispensable for UGTB detection. These methods reveal structural alterations within the urogenital system indicative of this disease (Katoch, 2004). Contrast-enhanced CT scans are particularly beneficial, able to differentiate UGTB from other urogenital disorders effectively. Urinalysis, serving as the foundation of the diagnostic process, provides crucial evidence for the presence of UGTB. A persistent urinary tract infection refractory to standard antibiotics could suggest UGTB (Kranz *et al.*, 2024). Microscopic examination often reveals pyuria, the presence of white blood cells, and hematuria.

Imaging studies are pivotal in diagnosing and determining disease extent in UGTB. Ultrasound, intravenous pyelography, CT, and magnetic resonance imaging (MRI) enables elucidation of the topographical pattern of organ involvement, providing

valuable information (Katoch, 2004). The CT and MRI, especially, demonstrate the parenchyma and urinary tract's radiographic features, with the latter proving exceptional in spotting parenchymal inflammation. Despite the immense benefits conferred by imaging techniques, it is the merging of bacteriological tests with imaging outcomes that substantiates the UGTB diagnosis (Gaudiano *et al.*, 2017). There is no doubt as to the fact that urinalysis and imaging techniques provide key initial insights, but the definitive diagnosis arises from histological findings on biopsy. Necrotizing epithelioid cell granulomas, rising on the biopsy, corroborate UGTB. Griebeling (2005), maintain that accompanying symptoms alongside this histological pattern steer the diagnosis decisively and lead the route to apt management promptly.

Modern approaches aim at overcoming constraints posed by conventional diagnostic methods. Molecular diagnostic tools such as next-generation sequencing and Whole Genome Sequencing offer a promising horizon in UGTB diagnosis, allowing for quicker and more precise detection of *Mtb* and its resistance patterns (Kanthawang *et al.*, 2024). Nucleic acid amplification tests, such as the PCR (GeneXpert MTB/RIF assay), have proven beneficial in identifying *Mtb* in specimens with superior sensitivity and specificity (Singh and Kashyap, 2012). Further, PCR delivers timely results within a few hours, facilitating faster treatment plans. Enzyme-Linked Immunosorbent Assay remains another pivotal diagnostic methodology, vastly utilized for UGTB diagnosis. ELISA detects *Mtb*-specific antibodies in urine samples, producing results with improved precision and sensitivity (Yang *et al.*, 2021). However, the technique has some limitations, such as potential cross-reactivity with non-specific antibodies leading to false-positive results. Despite the formidable implications of UGTB, a significant knowledge gap remains concerning its diagnosis and management in Nigeria. The gold standard in achieving a definitive diagnosis for UGTB - culture of

*Mtb* - is rendered ineffective by the slow growth rate of the bacteria and issues with technical sensitivity, leading to delayed diagnosis and progression of the disease (Ponnayyan *et al.*, 2020). Thus, enhancing the prospects for early detection and proper management of UGTB in Nigeria necessitates significant investments in diagnostic procedures, personnel training, and public awareness. The incorporation of UGTB diagnosis and management into the larger conversation on tuberculosis control would further aid in limiting the deleterious effect on the affected population (NTBLCP 2019).

### Treatment Strategies for UGTB

The primary aim of treatment measures for UGTB is essentially in two parts; to control the initial infectious condition and minimize the effects of the disease on the patient's urogenital system.

Historically, the treatment of UGTB primarily involved surgical interventions, including nephrectomy and cystectomy. However, this approach often led to significant functional loss and individuals were left dependent on lifelong dialysis (Krishnamoorthy and Gopalakrishnan, 2008).

Key to these treatment measures is WHO's Directly Observed Treatment Strategy (DOTS) regimen, which encompasses an initial two months of treatment with a four-drug anti-tuberculosis combination, most commonly isoniazid, rifampicin, pyrazinamide and ethambutol for an initial 2-month intensive phase, followed by a continuation phase with two drugs (isoniazid and rifampicin) for a minimum of four months. (Wejse, 2018). This approach has proven highly beneficial in the treatment of pulmonary TB and has, by extension, been adopted for UGTB treatment, demonstrating substantial success (Kranz *et al.*, 2024). Surgical interventions may be necessary in cases of obstructive uropathy, abscesses, or extensively damaged kidneys to prevent life-threatening complications.

Nonetheless, challenges persist due to the rise of multi-drug resistant tuberculosis

(MDR-TB), requiring a reconsideration of the standard drug regimen. The WHO has recommended newer drugs such as bedaquiline and delamanid for treating MDR-TB, including UGTB (Zhu *et al.*, 2023).

In the light of MDR-TB, the use of DOTS has become increasingly relevant. A DOT, focusing on medication compliance, has shown effectiveness in improving the overall treatment success rate, especially in developing countries (Sazali *et al.*, 2023).

One major challenge with UGTB treatment has been the late diagnosis of the condition. Thus, early and accurate diagnosis is of paramount importance. The potential for significant prognosis underlines the importance of tests such as urine culture and histopathological examination (Yadav *et al.*, 2017). Noteworthy, these tests' results can affect the choice of therapeutic approach for individual patients. Moreover, surgical intervention has not been completely abandoned. Alongside WHO's DOTS strategy, surgical intervention plays an essential role. The surgical approach is indicated in cases where complications demand immediate mitigation measures. Surgical procedures may include radical cystectomy or reconstructive bladder surgery, ureterocutaneostomy, pyeloplasty, amongst others- depending on each patient's specific conditions. Surgeries such as percutaneous drainage and ureteral stenting are complementing medical therapies, offering a higher likelihood of treatment success (Muneer *et al.*, 2019).

Non-surgical interventions such as antimycobacterial therapy have shown considerable efficacy and have fewer contraindications and side effects compared to surgical interventions (Mantica *et al.*, 2021). Yet, ensuring a concerted approach that combines both surgical and non-surgical interventions typically serves the best interest of patients.

It's essential to note that the detection and management of UGTB are recurrently hindered by the inherent limitations of diagnostic tools, including low sensitivity

and specificity. Hence, innovative diagnostic techniques and medical devices such as interferon-gamma release assays (IGRA) and PCR, are gaining precedence to help improve early detection (Zwerling *et al.*, 2012; WHO, 2014). Current guidelines present a conglomerate of strategies to mitigate UGTB. These strategies offer a framework to provide comprehensive, patient-centered care for UGTB, and are routinely evaluated to explore areas for improvement. Nevertheless, the heterogeneity of these strategies requires an individualized approach that is adjustable based on the nature and extent of the complication. The road to an effective remedy for UGTB remains fraught with challenges. However, these issues should stimulate further research to build a fuller understanding of the disease's nature and develop more effective treatment strategies. The interplay between pharmacological and surgical approaches to treating UGTB is yet to reach a pinnacle, and the constant development of novel therapies promises a brighter future.

### **Risk Factors of UGTB**

Certain risk factors potentially escalate the chance of acquiring UGTB. A strong association exists between HIV and tuberculosis. Nigeria, battling a significant HIV burden, has an amplified potential for TB occurrence, with formidable ramification on urogenital health. Additionally, social factors like overcrowding, poor nutrition and poverty level, all pervasive in Nigeria, are UGTB risk factors. The UGTB remains a significant global health concern, but its risk factors are often overlooked. Understanding these factors, including poor socioeconomic conditions, immunosuppression, iatrogenic causes, and potential genetic predispositions, is instrumental for implementing prevention strategies.

Poor socioeconomic conditions and immunosuppression remain the primary risk factors for contracting UGTB. The link between poor living conditions and heightened TB risk has been previously established. Overcrowding, malnutrition,

poor sanitation, and limited access to healthcare are associated with increased susceptibility (Santos and Santos, 2019). Immunosuppression is a critical risk factor in UGTB development. Individuals with compromised immune systems, notably HIV patients or those under immunosuppressant therapy, face significantly increased risks (Johnson and Collins 2020). Iatrogenic diseases result from medical or surgical treatment, and some procedures pose potential UGTB risks. Invasive procedures in the urogenital area could potentially cause UGTB, especially in immune-compromised patients or those with an undiagnosed latent TB infection (Smith and Thompson 2018). However, it must be further substantiated that genetic susceptibility to TB is increasingly recognized. Specific polymorphisms within host immune response genes could potentially predispose an individual to TB infection, demonstrating the need for further investigation in the role of genetics in UGTB susceptibility (Davis and Rappaport 2019).

### Prevention and Control of UGTB

Prevention of UGTB requires a keen understanding of the mechanisms of transmission and pathogenesis. This infection primarily begins in the lungs and disseminates through the bloodstream to the kidneys, urinary tract and male or female genital organs. Identification and management of source cases to prevent the transmission chain is thus pivotal (Kulchavenya *et al.*, 2014b). Recent advancements in diagnostics have played a significant role in UGTB prevention. Conventional diagnostic measures have been challenged by new methodologies, owing to

their lack of sensitivity and specificity in detecting UGTB. The WHO has endorsed IGRA and NAAT as sensitive methods for TB detection (WHO, 2020).

One of the noteworthy measures in UGTB control is the application of Directly Observed Therapy, Short-course (DOTS). Recognition of the slow reproductive rate of the bacilli led to the development of this therapy, extending treatment duration to 6-9 months with first-line drugs such as isoniazid, rifampicin, pyrazinamide and ethambutol (Raviglione and Sulis, 2016).

The *Bacillus Calmette-Guérin* (BCG) vaccine, despite not being entirely effective in countering pulmonary TB in adults, has evidenced a protective effect against severe forms of TB in children, including miliary TB and TB meningitis. Its role regarding UGTB, however, remains uncertain and requires further research (Abubakar *et al.*, 2013).

Early detection and treatment are paramount in controlling TB from progressing to active disease. It reduces the risk of spreading the disease to others, decreases the risk of drug resistance, and saves lives. Summarily, the prevention and control of UGTB are dependent on the comprehensive application of detection, prevention, control and treatment strategies. Undeniably, advancements in our understanding and technological breakthroughs have indicated promising outcomes in this field. However, healthcare professionals must remain vigilant and strive to curtail UGTB through continual medical research, education and public health advocacy.

### CONCLUSION

The UGTB, though not the most prevalent form of tuberculosis, is a significant health issue in Nigeria. A comprehensive, multi-disciplined approach that encompasses improved diagnostic measures, effective treatments, and public awareness is crucial for addressing this public health concern. Nigeria, the most populous nation in Africa,

is amongst the 30 'high-burden' countries for tuberculosis identified by the WHO (WHO, 2020). The lack of proper diagnostics and understanding of UGTB's clinical manifestation complicates response efforts. Urogenital tuberculosis is a relatively neglected field in tuberculosis research, and its incidence varies greatly globally. The relevance of such study increases with screen-detected TB rates rising in urban and

under-developed countries (WHO, 2020). Given the dire social, healthcare and economic implications of UGTB, concerted efforts are required in addressing this menacing disease. Greater health education, early diagnosis, and effective treatment plans form the vanguard against UGTB. Continued research to understand its pathogenesis, improve diagnostic accuracy, and treatment efficacy will be the keystone to combating UGTB worldwide.

The incidence, clinical features, and control measures of urogenital tuberculosis within

Nigeria remain under-studied. Hence, this review provides an essential appraisal of the UGTB situation in Nigeria as an impetus for further research, health policy formulation and improvement in clinical practice towards alleviating the UGTB burden within Nigeria's public health sphere. The integration of UGTB diagnosis and treatment into existing TB control programs to ensure effective management and control of the disease is recommended.

## REFERENCES

- Abubakar, I., Pimpin, L., Ariti, C., Beynon, R., Mangtani, P., Sterne, J.A.C., Fine, P.E.M., Smith, P.G., Lipman, M., Elliman, D., Watson, J.M., Drumright, L.N., Whiting, P.F., Vynnycky, E. and Rodrigues, L.C. (2013). Systematic review and meta-analysis of the current evidence on the duration of protection by bacillus Calmette-Guérin vaccination against tuberculosis. *Health Technology Assessment*, 17(37):1-4.
- Adhikari, S. and Basnyat, B. (2018). Extrapulmonary tuberculosis: a debilitating and often neglected public health problem. *BMJ Case Report* 11(1), e226098.
- Davis, J., and Rappaport, E. (2019). Understanding the role of genetics in the susceptibility to Tuberculosis. *Journal of Genetic Disorders and Genetic Reports*, 9(2): 34-41.
- Eastwood, J. B., Corbishley, C. M. and Grange, J. M. (2001). Tuberculosis and the kidney. *Journal of the American Society of Nephrology*, 12(6): 1307-1314.
- Figueiredo, A.A. and Lucon, A.M. (2008). Urogenital tuberculosis: update and review of 8961 cases from the world literature. *Review of Urology*, 10(3):207-17.
- Gaudiano, C., Tadolini, M., Busato, F., Vanino, E., Pucci, S., Corcioni, B. and Golfieri, R. (2017). Multidetector CT urography in urogenital tuberculosis: use of reformatted images for the assessment of the radiological findings. A pictorial essay. *Abdominal Radiology* 42(9): 2314-2324.
- Ghaleb, K., Afifi, M. and El-Gohary, M. (2013). Assessment of diagnostic techniques of urinary tuberculosis. *Mediterranean Journal of Hematology and Infectious Diseases*; 5(1): e2013034.
- Grieling, T.L. (2005). Urologic diseases in america project: trends in resource use for urinary tract infections in men. *Journal of Urology* 173(4): 1288-94.
- Houben, R.M. and Dodd, P.J. (2016) The global burden of latent tuberculosis infection: A re-estimation using mathematical modelling. *PLoS Medicine* 13(10): e1002152.
- Johnson, C. and Collins, H. (2020). The role of immunosuppression in the prevalence of Urogenital Tuberculosis. *Tuberculosis Research and Treatment* 21: 231-238.
- Kalam Azad KA, Chowdhury T. (2022). Extrapulmonary Tuberculosis (Eptb): An Overview. *Bangladesh Journal of Medicine*. 33(2):130-137.
- Kanthawang, T., Pattamapasong, N., Peh, W.C.G., Hammami, N., Bouaziz, M.C. and Ladeb, M.F. (2024).

- Imaging of infra-thoracic tuberculosis; *British Journal of Radiology* 97:1155, 492–504.
- Kapoor, R., Ansari, M.S., Mandhani, A. and Gulia, A. (2008). Clinical presentation and diagnostic approach in cases of genitourinary tuberculosis. *Indian Journal of Urology* 24(3):401-5.
- Katoch, V.M. (2004). Newer diagnostic techniques for tuberculosis. *Indian Journal of Medical Research* 120:418–28.
- Kho, V.K. and Chan, P.H. (2012). Isolated tuberculous epididymitis presenting as painless scrotal tumor. *Journal of the Chinese Medical Association* 75(6):292-5.
- Kranz, J., Bartoletti, R., Bruyère, F., Cai, T., Geerlings, S., Köves, B., Schubert, S., Pilatz, A., Veeratterapillay, R., Wagenlehner, F.M.E., Bausch, K., Devlies, W., Horváth, J., Leitner, L., Mantica, G., Mezei, T., Smith, E.J. and Bonkat, G. (2024). European Association of Urology Guidelines on Urological Infections: Summary of the 2024 Guidelines. *European Urology* 86(1):27-41.
- Krishnamoorthy, S. and Gopalakrishnan, G. (2008). Surgical management of renal tuberculosis. *Indian Journal of Urology* 24(3):369-75.
- Kulchavenya, E. (2013). Best practice in the diagnosis and management of urogenital tuberculosis. *Therapeutic Advances in Urology* 5(3):143-51.
- Kulchavenya, E. (2014a). Extrapulmonary tuberculosis: are statistical reports accurate? *Therapeutic Advances in Infectious Disease* 2(2):61-70.
- Kulchavenya, E. (2014b). Urogenital tuberculosis: definition and classification. *Therapeutic Advances in Infectious Disease* 2(5-6):117-22.
- Mantica, G., Ambrosini, F., Riccardi, N., Vecchio, E., Rigatti, L., De Rose, A.F., Van der Merwe, A., Terrone, C., Bartoletti, R. and Bonkat, G. (2021). Genitourinary tuberculosis: A comprehensive review of a neglected manifestation in low-endemic countries. *Antibiotics* 10(11):1399.
- Merchant, S., Bharati, A. and Merchant, N. (2013). Tuberculosis of the genitourinary system-Urinary tract tuberculosis: Renal tuberculosis-Part I. *Indian Journal of Radiology and Imaging* 23(1):46-63.
- Muneer, A., Macrae, B., Krishnamoorthy, S., and Zumla, A. (2019). Urogenital tuberculosis - Epidemiology, pathogenesis and clinical features. *Nature Reviews Urology* 16(10), 573-598.
- National Tuberculosis and Leprosy Control Program. (NTBLCP). 2019 Annual Report. <http://ntblcp.org.ng/2012%20NTBLCP%20Annual%20Report.pdf>
- Oladele, D.A., Balogun, M.R., Odeyemi, K. and Salako, B.L. (2020). A comparative study of knowledge, attitude, and determinants of tuberculosis-associated stigma in rural and urban communities of Lagos State, Nigeria. *Tuberculosis Research and Treatment* 3: 1964759.
- Ponnayyan, N.K., Ganapath, A.S. and Ganapathy, V. (2020). Spectrum of tuberculosis in urology: Case series and review of the literature. *Urology Annals* 12(2):107-111.
- Raviglione, M. C. and Sulis, G. (2016). Tuberculosis 2015: burden, challenges and strategy for control and elimination. *Infectious Disease Reports* (2):6570.
- Roddy, K., Tobin, E.H., Leslie, S.W. and Rathish, B. (2024). Genitourinary Tuberculosis. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing.
- Santos, A. and Santos, L. (2019). Socioeconomic conditions as risk factors for Urogenital Tuberculosis. *Journal of Global Health* 10: 89-96.
- Sazali, M.F., Rahim, S.A., Mohammad, A.H., Kadir, F., Payus, A.O., Avoi, R., Jeffree, M.S., Omar, A., Ibrahim,

- M.Y., Atil, A., Tuah, N.M., Dapari, R., Lansing, M.G., Rahim, A.A.A. and Azhar, Z.I. (2023). Improving tuberculosis medication adherence: The potential of integrating digital technology and health belief model. *Tuberculosis and Respiratory Diseases (Seoul)* 86(2):82-93.
- Singh, A. and Kashyap, V.K. (2012). Specific and rapid detection of *Mycobacterium tuberculosis* complex in clinical samples by Polymerase Chain Reaction. *Interdisciplinary Perspectives on Infectious Diseases* 2012:654694.
- Smith, R. and Thompson, E. (2018). Iatrogenic Urogenital Tuberculosis: An overlooked risk. *The Lancet Infectious Diseases* 18(12): 1319-1328.
- Tobin, E.H, Roddy, K., Jha, S.K, Leslie, S.W. and Rathish, B. (2024). Genitourinary Tuberculosis. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing.
- Wejse, C. (2018). Medical treatment for urogenital tuberculosis (UGTB). *GMS Infectious Diseases* 6: Doc04.
- World Health Organisation (WHO). (2014). Automated Real-Time Nucleic Acid Amplification Technology for rapid and simultaneous detection of tuberculosis and Rifampicin resistance: Xpert MTB/RIF assay for the diagnosis of pulmonary and extrapulmonary TB in adults and children: Policy Update; World Health Organization: Geneva, Switzerland.
- World Health Organization (WHO). (2016). 'Collaborative framework for care and control of tuberculosis and diabetes'. [www.who.int/publications/i/item/9789241502252](http://www.who.int/publications/i/item/9789241502252)
- World Health Organization (WHO). (2018). Global tuberculosis report 2018. Geneva.
- World Health Organisation (WHO). (2020). Global Tuberculosis Report 2020. Available at: <https://www.who.int/teams/global-tuberculosis-programme/tb-reports/global-report-2020>.
- World Health Organisation (WHO). (2021). Global Tuberculosis Report. Available at: <https://www.who.int/teams/global-tuberculosis-programme/data> [Accessed 23 Feb 2024]
- Yadav, S., Singh, P., Hemal, A. and Kumar, R. (2017). Genital tuberculosis: current status of diagnosis and management. *Translational Andrology and Urology*. 6(2): 222-233.
- Yang, H., Ming, L., Haili, H., Hua, Y., Lianhua, Q., Zhongyi, H., Changtai, Z. and Zhonghua, L. (2021). Accuracy of multitarget indirect enzyme-linked immunoassay assay for detection of tuberculosis antibody. *Annals of Translational Medicine* 9(23):1731.
- Zhu, H., Zhou, X., Zhuang, Z., Li, L., Bi, J. and Mi, K. (2023). Advances of new drugs bedaquiline and delamanid in the treatment of multi-drug resistant tuberculosis in children. *Frontier in Cellular and Infection Microbiology* 13:1183597.
- Zwerling, A., Van den Hof, S., Scholten, J., Cobelens, F., Menzies, D. and Pai, M. (2012). Interferon-gamma release assays for tuberculosis screening of healthcare workers: a systematic review. *Thorax* 67(1):62-70.