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Urogenital Tuberculosis in the Niger Delta region of southern Nigeria: Our experiences, challenges, features and outcome

Monday Komene Sapira [1,*] and Vitalis Obisike Ofuru [2]

[1] *Department of Surgery, University of Port Harcourt Teaching Hospital, Port Harcourt, Rivers State, Nigeria.*
[2] *Urology Unit, Department of Surgery, University of Port Harcourt Teaching Hospital, Port Harcourt, Nigeria.*

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Abstract

Introduction: Tuberculosis (TB) has high morbidity and mortality. It's prevalent in Niger Delta Region of Nigeria but urogenital TB (UGTB) appears neglected in the region. We present our 17-year experiences, challenges in diagnosis and treatment of UGTB in Port Harcourt, a centre for TB treatment in the region.

Materials Methods: Consecutive urology patients managed at University of Port Harcourt Teaching Hospital (UPTH), Nigeria (1/1/2005-31/8/2022) were evaluated. Those with provisional diagnosis of UGTB were further investigated with confirmatory and staging tests for TB, including Gene Expert Ultra studies and histopathology. Patients with diagnosis of UGTB were given anti-tuberculous chemotherapy, operated surgically as indicated, and had active surveillance. Data were collected contemporaneously with management of patients and collated with simple statistics.

Results: Total of 36,176 were evaluated. Nine (9) had diagnosis of UGTB and here reported. Hospital incidence of UGTB was 25 /100000 patients' population. Four (4) patients were male and 5 female. Mean age at presentation (years) was 46.5 ±.9.7, and age range 23-79. Fi**ve** female and 1 male patients had kidney TB (KTB); and 1 pulmonary TB with TB cysto-prostatitis. Four patients presented with grades 3 and 4 KTB, nephrolithiasis and multiple pus-laden renal cysts.

Conclusion: UGTB is common in the region but confirmatory diagnostic tests lack good sensitivity. Patients presented late with high disease burden and often required surgical intervention. Combinations of high index of suspicion, clinical assessment with non-confirmatory/confirmatory tests are the currently available tools for diagnosis of UGTB. Recommendations are given on anti-tuberculous chemotherapy and surgery.

Keywords: Challenges; Features and outcome; Urogenital tuberculosis; Niger Delta Region; Nigeria

1. Introduction

Tuberculosis (TB) has been declared a global health problem by the World Health Organization with about one-third of the world population being infected [1]. The disease is associated with high morbidity and mortality. Nigeria is one of the 27 countries world-wide with high burden of TB [2]. In a study on an HIV – negative population of subjects in the country, a high prevalence of 27% and an incidence rate of 158/100,000 population, and a total 2016 tuberculosis cause-specific mortality of 39,933 were observed [3]. At University of Port Harcourt Teaching Hospital [UPTH], Port Harcourt, Nigeria, HIV-associated PTB has been known to cause 16.23%(n=124) of non-maternal deaths in women of reproductive age(15-49 years); PTB alone caused 1.51%(n=124) [4]. In many parts of the country, multidrug resistant (MDR) strains had since emerged with different studies reporting MDR-rates of 3.3% [2]; and "2.9% of newly diagnosed TB patients and 14% of retreated ones" [5].

* Corresponding author: Monday Komene Sapira; Email: monday.koesi@gmail.com
Department of Surgery, University of Port Harcourt Teaching Hospital, Port Harcourt, Nigeria.

In highly endemic communities, urogenital tuberculosis (UGTB) is the second most common form of extra-pulmonary tuberculosis (EPTB) after TB of lymph nodes [6]. Considerable efforts have been made in the Niger Delta Area in prevention, early diagnosis and treatment of tuberculosis. However, co-ordinated efforts and TB control programs are scarcely in the important areas of prevention, early diagnosis, treatment and documentation of urogenital TB (UGTB). We present our experiences within a period of 17 years in the management of urogenital TB in Port Harcourt [PHC], a treatment center for TB in the Niger Delta Region of Nigeria.

2. Patients and Methods

This study was carried out on patients seen at the Urology Division of UPTH during outpatient clinic consultations which were held every Monday (4 days/ month). They also included patients seen at the Accidents and Emergency Departments and other departments of the hospital, usually referred for urological service, as well as referrals from neighboring states and health institutions. Patients were seen during their routine hospital services. Patients diagnosed with UGTB and treated between January, 2005 and August, 2022 were included in the study. Data were collected contemporaneously with clinical evaluation, investigation, treatment and follow up of consecutive patients. When necessary, additional data were retrieved from patients' case files, admission and discharge registers and histopathological report notes. Data collected included age, place of origin, local government area of origin, occupation and referral hospitals (for patients referred to UPTH from other institutions or states). Dates of admission and discharge, presenting complaints of the patients, duration of symptoms and associated symptoms were noted. Notes were taken of patients with previous tuberculosis (TB), and contact with TB patient(s). The level of care received before presentation and the complications developed were also documented. Relevant past medical, surgical/ obstetrics and gynecology histories were noted as well as family and personal history of pulmonary tuberculosis. Detailed observations on general and systemic physical examinations of each patient were recorded. Laboratory investigation results and treatments received were also documented. Patients diagnosed with tuberculosis were given neoadjuvant anti-tuberculous chemotherapy, except when contraindicated, before indicated elective surgery for TB complications. This included daily oral rifampicin 600mg, isoniazid 300mg, pyrazinamide 1g ethambutol 800mg and pyridoxine for the first 2 months with active surveillance at the Infectious Diseases Clinic of the hospital, and continuing oral rifampicin and isoniazid for another 12 months. Supportive treatment included treatment of cardiovascular, metabolic and pulmonary comorbidities- congestive heart failure, diabetes mellitus and hypertension. Basic observations of frailty levels, O_2 saturation, and performance status were made. Pre-operative evaluation of history of renal dysfunction and serial biochemical assay of renal function [using serum urea, creatinine, electrolytes and bicarbonate assay] were done. We crosschecked this with estimation of GFR using the MDRD formula [7] where necessary. Assessments of contra-Iateral renal anatomy and renal function, using available ultrasound scan (USS) and CT-urography [CTU] or intravenous urography [IVU] in selected patients were made. Patients that required surgery were preoperatively prepared. The present study does not contain any experiments performed on animal/human subjects by any of the authors. Informed consent was obtained from all individual patients included in the study. Separate consents for surgery and anaesthesia were obtained. Operations were done in compliance with standard procedures. Operative findings were recorded and relevant aspects included in this report.

3. Results

The Urology Unit (UPTH) at which this study was done had an average of four (4) outpatient clinics monthly, treated 36176 patients during the study period. Nine (9) patients were diagnosed with urogenital tuberculosis (UGTB). This gave a hospital incidence rate of 25 patients with UGTB per 100,000 patients' population during the study period. Four (4) were male and 5 female (male- to-female ratio, 1:1.25). Four (4) of the females were women of reproductive age (WRA) (15 to 49 years). Ages of all the 9 patients (in years) ranged between 23 to 79, median 40, and mean of 46.5± 9.7. Six (6) patients (five females and one male) had kidney tuberculosis (KTB), two tuberculosis of the epididymis (EPDTB), while one presented with pulmonary tuberculosis (PTB) with tuberculosis of the urinary bladder (UBTB) and prostate. Of patients with KTB, four (4) were from two local high institutions; another with EPDTB was a lecturer in one of these two institutions. Diagnosis of tuberculosis (TB) in one patient with PTB and urinary bladder TB cystitis was by the Gene Expert Ultra System. The patients had a mean delay (in months) of 10.24 (median 3 months, and a range of 0.17 to 36.00 months) in reporting to a health facility for treatment.

3.1. Presentation of case Series

3.1.1 Patient No. 1

A 37-year old petty trader who hailed from a neighboring state and lived in a suburb of Rivers State, Nigeria. She was admitted into the Urology Ward from UPTH Accidents and Emergency Department. She presented with constant,

moderate-to-severe left lumbar [loin] pain of 2 months duration, progressive left lumbar swelling, weight loss and loss of appetite, all of the same duration. There was no history of fever, gross hematuria, drenching night sweats, TB or contact with patients having TB. She was happily married, with 2 children and had no family history of pulmonary tuberculosis. She was middle-aged, ill-looking and pale. She had a firm, immobile, tender left lumbar mass that extended to the umbilicus and moved with respiration.. Other systems were essentially normal.

Preliminary diagnosis of left renal tumor was made. Abdominal ultrasound scan showed massively enlarged and echo-complex left kidney harboring multiple calculi. A second sonographer's opinion was sought and the report was suggestive of left multicystic kidney disease. The right kidney was normal in both reports. Abdominal CT scan revealed a large heterogeneous left kidney that showed excretory function in its thinned cortex. Serial Renal Function Tests were all normal. While the patient was still being investigated, there was spontaneous discharge of pus from the swelling through an opening in the left lumbar region. Microscopy [Ziehl Neelsen test] of this effluent revealed pus cells but no alcohol and acid fast bacilli (AAFB) were seen. Culture of the effluent yielded staph aureus that was sensitive to ceftazidime and ofloxacin. Urinalysis showed many pus cells per high power field [pyuria], mild proteinuria, organisms (++), epithelial cells, and leucocyturia (++) as the only positive findings. Full blood count showed normal indices and serial haemogram was consistently above 9g/dl. Serology for HIV1and2, HBsAg and HCV were all seronegative. Result of VDRL test was nonreactive. Liver function test also showed the liver had no abnormalities. The renal abscess was drained. Cysts were marsupial zed and calculi removed.

Operative findings included multiple peripheral cortical renal parenchymal abscesses, each of which communicated with the renal pelvis. Calculi were found in the renal pelvis and in abscess cavities. The parenchyma was friable and fragmented with ease. Cheesy pus with characteristic offensive odour was drained. There was a mass consisting of retroperitoneal inflamed tissues surrounding the major vessels. A draining sinus was also noted. Section of the abscess cavity was excised for histology and a non-active tubular drain put in place. Smear test on the aspirate yielded no AAFB. Histology showed chronic inflammatory mass. Post operatively, pussy discharge remained copious despite broad spectrum antibiotic combination with metronidazole, meropenem, and gentamicin. A presumptive diagnosis of left kidney TB was then made and antituberculous treatment commenced. Progressive improvement was noted in the patient's clinical state until discharge, about 4 weeks after commencement of anti TB drugs. At follow-up to 3 months, the patient had made good clinical recovery with no fresh complaints.

3.1.2 Patient No. 2

A 25-year old female undergraduate, an indigene and resident of a neighboring South Eastern Region of Nigeria. She presented with high grade, intermittent fever with chills of 10 days duration and dull right flank pain of 4 days duration which radiated to the umbilical region. There was associated nausea and vomiting. Six days into her illness, she noticed pus in her urine but there was no history of hematuria or lower urinary tract symptoms. There was no history of chronic cough, previous TB, drenching night sweat or contact with a patient with TB, weight loss or anorexia. She was the last child in a family of 7 children. There was no family history of tuberculosis.

At presentation she was acutely ill, had a temperature of 38^{o}c, pulse rate of 102 per minute, and respiratory rate of 24 cycles/minute. There was right renal angle tenderness but the kidneys were not ballot able. Abdominal organs were not palpably enlarged. Rectal examination was unremarkable. A provisional diagnosis of right renal abscess was made. Abdominal ultrasound revealed an enlarged right kidney harboring multiple cystic masses with increased echotexture. The largest, which measured 5.2cm x 4.0cm was located in the superior pole, and the smallest [2.0cm x 2.2cm] was located in the inferior pole. There was poor corticomedullary differentiation. The left kidney was normal in size, measuring 9.8cm x 6.2 cm with no pelvicalyceal collection or renoliths. Mantoux test was negative. Full blood count gave normal results. ESR was 125mm/first hour [Westergreen]. Results of urinalysis, urine culture and serology and IVU were essentially normal. He has so far shown marked improvement in clinical state on preliminary ant tuberculous chemotherapy. She is being prepared for renal surgery.

3.1.3 Patient No.3

A 75-year old retired professor, who presented with storage lower urinary tract symptoms and swelling in the right hemi-scrotum of three (3) months duration. Examination revealed an enlarged prostate that appeared benign clinically. The right epididymis was swollen and adherent to the ipsilateral testis. It was irregular and hard with mild tenderness. Serum α- fetoprotein and β-HCG were within the normal reference range. Full blood count showed normal results except ESR which was 35mm/first hour (Westergreen). Mantoux test was 13mm positive after 48 hours. Ziehl- Neelsen smear test on urine for acid-fast bacilli (AFB) was negative for three consecutive days. Patient was placed on medical treatment for benign prostatic enlargement [BPH] and antibiotics for right epididymoorchitis but there was no improvement in

symptoms. A presumptive diagnosis of tuberculous epididymitis was made with TB Prostate as differential. Biopsy of the epididymal lesion was not made on suspicion that it might be malignant.

The patient was commenced on anti-tuberculous therapy with improvement of his clinical state. The scrotal lesion regressed progressively and patient showed sustained improvement over a follow up period of 3 months. In appreciation of his improved clinical state, he donated a copy of his book to the first author.

3.1.4 Patient No.4

A 23-year old undergraduate female student who lived in a middle density part of PHC. She was seen in the Urology Clinic with a 5-day history of total painless hematuria. There was no history suggestive of clotting abnormalities or use of anticoagulants. However, she had malaise, weight loss, frequent micturition, nocturia and dysuria. She had neither previous personal nor family history of TB. She was ill-looking, young, and afebrile. She had no peripheral oedema or pallor. Her vital signs were stable. There was no renal angle tenderness. No abdominal organ was palpably enlarged.

A preliminary diagnosis of bladder urothelial tumor was made. Her packed cell volume [PCV] was 28%, and ESR 24mm/ first hour [Westergreen]. Erythrocytes on blood film had hypochromia and anisocytosis but platelets were adequate morphologically. Clotting profiles had essentially normal results.

She had marked erythrocyturia and sterile pyuria. Urine cytology revealed no evidence of malignancy. Mantoux test was 16mm reactive. Chest plain radiographic examination revealed no focal lung lesions. Both intravenous urography (IVU) and abdominal CT-scan revealed no abnormalities.

Findings at Cystoscopy were normal external urethral meatus with vulvar mucosal excoriations and coloration with flakes of yellow-white discharge. Trigone was congested and hyperemic. Left ureteric orifice was normal in shape and size but spotting frank red blood. Right ureteric orifice had a ridge medially. There were prominent mucosal veins. A presumptive diagnosis urogenital tuberculosis [UGTB] was made and patient was placed on empirical anti tuberculous drugs. A follow-up two weeks later showed he improved on this therapy. He is still being followed up with treatment and active surveillance.

3.1.5 Patient No. 5

This was a 40-year old male police constable referred from Police Clinic on grounds of progressive irreducible left hemi-scrotal swelling of 3 years duration. Swelling was initially painless but later became painful. There was no history of trauma, fever or TB. There was no history of sexually transmitted infections or previous testicular torsion. He had frequent micturition.

He was a young man in no painful distress. His pulse rate was 80/min and blood pressure 150/80mmHg. Abdominal examination revealed no abnormalities. His phallus was normal. The right hemi-scrotum and its contents were essentially normal. However, he had a cystic mass in his left hemi-scrotum. The mass was inferior and separate from an apparently normal ipsilateral testis. The mass measured 5cm by 6cm, was firm and tender. We could get above it. Tran's illumination sign was negative. Digital rectal examination revealed an apparently normal prostate. A provisional diagnosis of left vaginal hydrocele to rule out left epididymal cyst was made. Results of full blood count [FBC] were normal. Fasting blood sugar was 5.0mmol/L and serum prostate-specific antigen [serum PSA] 3ng/ml. Findings on abdominal and scrotal ultrasonography [USS] were normal right testis; left testis was also normal but the tunica vaginalis contained debritic fluid. There were no varicoceles bilaterally. The ultrasound diagnosis was infected hydrocele. Mantoux test was positive 16mm positive. Diagnosis of Tuberculous epididymitis was made and patient was placed on anti-tuberculous drugs. He made progressive and sustained clinical recovery. He is still on treatment with active surveillance and possible excision biopsy of the scrotal cyst.

3.1.6 Patient No.6

This patient was male, aged 79 years, retired civil servant who presented to the Urology unit for treatment with complaints of difficulty in passing urine for previous 6 months. He had frequency, urgency, urge incontinence a weak streams of urine during micturition. He also had cough productive of altered white sputum with hemoptysis.

He was chronically ill looking, anicteric with moderate pallor. His respiratory rate was 22 cycles per minute. He had coarse crepitation over the middle and upper zones of both lungs. He was in chronic urinary retention with distended urinary bladder.

Rectal examination revealed that his prostate gland was enlarged and firm with marked tenderness. A provisional diagnosis of pulmonary tuberculosis, chronic retention of urine due to prostatic TB was made. Urethral stricture disease was also suspected.

His PCV (hematocrit) was 25%, platelet 281x10^9/L WBC was 12.9x10^9/L; ESR=140 mm/first hour (Westergreen). His serum electrolyte concentrations [mmol/L] were sodium 128, potassium 3.8, and bicarbonate 24.0; Urea 3.4 mmol/L and creatinine 55 μmol/L. Serum prostate-specific antigen level was 3.0mg/ml. **Urinalysis:-** His urine was amber and cloudy with specific gravity 1.015. It had markedly significant pyuria [numerous pus cells/ high power field [hpf] and significant microscopic hematuria [erythrocytes 4-6/hpf]. Other urinalysis results were casts-nil, bacterial cells+, glucose negative, proteins 30mg/dl, blood 25 Ery/μL; leucocyturia of 75 Leucocytes /μL. Nitrites, ketones, bilirubin and urobilinogen were negative. Urine culture yielded heavy growth of E.coli sensitive to meropenem, but partially susceptible to Augmentin® and ampicillin. On abdominopelvic ultrasonography, his liver span was12.4cm, normal size and echotexture. His gall bladder was normal. Kidney lengths were 9.6 cm (Left), 9.7cm (right). Kidney cortico-medullary differentiation was normal. The spleen had greatest dimension of 11cm with normal parameters. The urinary bladder had thickened walls, with features of cystitis.

Plain chest X-ray examination done third day of evaluation showed that he had reticulonodular opacities with background cystic cavity changes in the upper middle lung zones bilaterally but worse on the left. There was marked reduction of the volume of the left Lung with ipsilateral mediastinal shift, There was blunting of the costo-phrenic angles. Heart size was normal. He had scoliosis of the thoracic spine with convexity to the left. The findings were in keeping with pulmonary tuberculosis, TB cysto-prostatitis. Sputum Gene Expert MTB-RIF Ultra test detected Mycobacterium tuberculosis (MTB) with moderate rifampicin (RIF) resistance. He had a course of intravenous meropenem 1g 8-hourly for 5 days, relief of chronic urinary retention with supportive treatment, followed by ant tuberculous therapy. He is doing remarkably well with 16 weeks of follow up.

3.1.7 Patient No. 7

This was a 33-year old post-graduate student, indigene of a neighboring state in the Niger Delta. He presented with history of recurrent colicky pains in his left loin for about 1 year before presentation. He had similar pains at the same site about 3 years previously. He was then evaluated and found to have an infective left renal tumor which was operated at a university teaching hospital in his state of origin. Referral notes indicated that intra operative findings in his previous hospital were left kidney enlargement with pus-containing multiple cysts. The cysts were incised, pus drained. He was treated with antibiotics; his clinical state improved.

One year later he had recurrent symptoms of left loin pains, intermittent fever, progressive weight loss, anorexia and an increasing left loin mass. He presented at UPTH for treatment as he could no longer continue his academic studies at the university.

He was chronically ill-looking, asthenic, afebrile, anicteric with moderate pallor. His chest was clinically clear. He had an irregular left lumbar mass which was bimanually palpable, tender with an irregular surface. The mass was 12cm x 10cm in transverse and longitudinal dimensions respectively**. Abdominal ultrasonography** confirmed the mass to be the left kidney which was enlarged, echo- complex with multiple cystic cavities. The right kidney had normal size and cortico-medullary differentiation. Intravenous urography revealed delayed contrast excretion, enlargement, calyceal dilatation and multiple opacities in the left kidney. The right kidney appeared normal. Serum electrolyte urea and creatinine levels were within normal limits.

A provisional diagnosis of recurrent left renal tumor (differential diagnosis of left renal cell carcinoma) was made. He had left kidney exploration. Intra-operative findings included an enlarged macroscopically benign-looking left kidney with multiple cysts containing foul-smelling cheesy pus. An aspirate of the pus yielded no acid and alcohol-fast bacilli (AAFB) on Ziehl-Nelseen (ZN) staining. The cystic cavities were incised, drained of pus and marsupial zed. Then the wound was closured. Intraoperative left renal biopsy was histologically diagnosed as a benign inflammatory mass. Culture of the pus yielded mixed growths of coliforms.

In the immediate post-operative period he was placed on intravenous ceftazidime 1g 12-hourly and metronidazole 500mg 8-hourly for 5 days based on antimicrobial susceptibility testing. His immediate post-operative recovery was not satisfactory. On clinical suspicion of left renal TB, based on clinical features, macroscopic features of the pus and intraoperative findings he was placed on presumptive anti tuberculosis chemotherapy. He made good clinical recovery, completed his postgraduate programme and went back to his state of origin. He has since been lost to follow- up after a 10-month period of active surveillance.

3.1.8 Patient No. 8

This patient was a 60-year old female from a neighboring state, referred to the Urology Clinic of UPTH with complaints of loin pains for approximately 3 months before presentation. The pain was deep-seated, colicky and intermittent. She also had a history of similar and recurrent abdominal pains 47 years previously, associated with constipation in the past for which she had abdominal operations as follows:- In 1974 (47 years previously) she had appendectomy for acute appendicitis. In 1975, 2008 and 2014 respectively she also had repeated laparotomies, intestinal resections and anastomoses at a private clinic for intestinal obstruction. There were no lower urinary tract symptoms or gross hematuria. She had previous diagnosis of vitreous detachment of the left eye at UPTH.

She was ill-looking, with moderate-to-severe level of frailty, afebrile, pale and anicteric. No peripheral pitting oedema. The abdomen was full, moved with respiration and had mid-line incisional scar, a right para median incisional scar; both scars were tender. Percussions over the renal angles were tender bilaterally. There was no palpable organomegaly but she had a doughy tenderness on percussion of the hepatic area. Intravenous urography showed she had bilateral renal stones and bilateral calyceal dilatation. Abdominal ultrasonography revealed hyperechoic lesions with distorted renal corticomedullary differentiation in both kidneys. Serial serum electrolytes, urea, bicarbonate and creatinine levels were within normal reference ranges. A presumptive diagnosis of bilateral advanced kidney tuberculosis (complication of abdominal TB) was made. She was commenced on anti-tuberculous chemotherapy with supportive treatment. She is scheduled for bilateral renal exploration after being optimized for surgery. She has done well on preliminary conservative treatment.

3.1.9 Patient No.9

This was a 46 - year old female referred to UPTH Urology unit from Federal Medical Centre (FMC) in a neighboring state. She had secondary level of education. She presented to the Urology Clinic with complaints of right loin pain of 5 months duration. Before presentation she developed persistent fever with rigors for 2 weeks. There were no loin swellings, history of hematuria or lower urinary tract symptoms. She had caesarean sections for her two deliveries, and evacuation for an incomplete abortion. The second caesarean section was in 2010. She was ill-looking. Her abdomen was full, had a midline sub-umbilical scar and mild-to-moderate tenderness on percussion of the renal angles. Her kidneys, liver and spleen were not palpably enlarged. There was no intra-abdominal palpable mass.

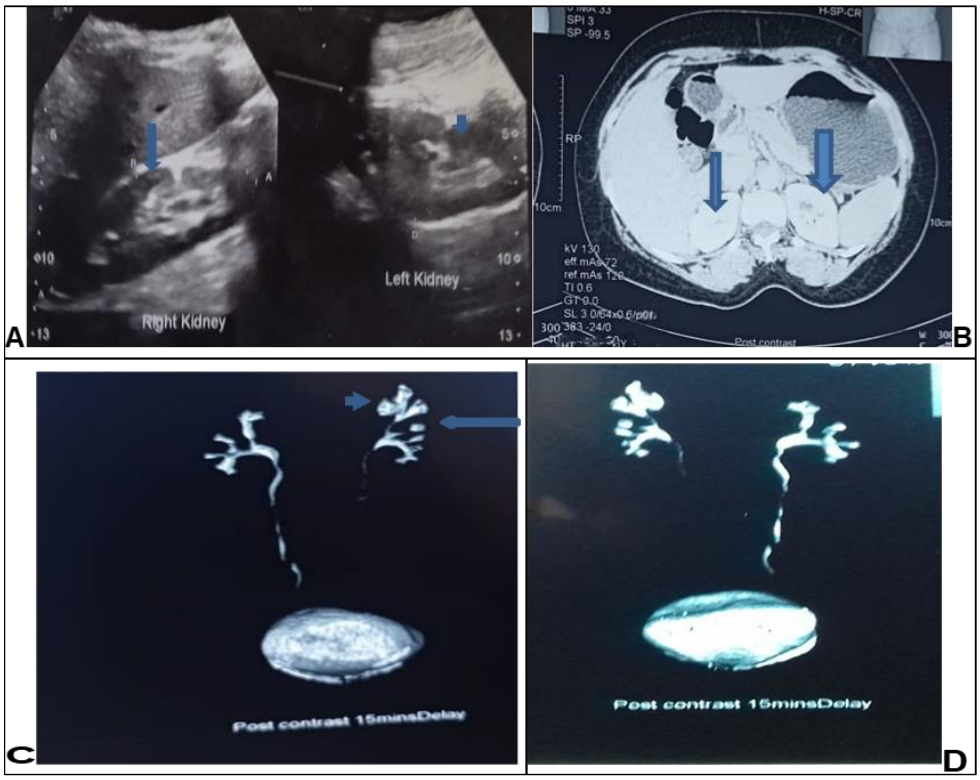

Figure 1A-D: Patient Number 9, Grade 2 Kidney TB: A, Ultra sonography of left kidney, and right kidney (longitudinal view sonograph), blue arrows. There is normal cortical thickness with good corticomedullary differentiation. No cysts observed; B, Transverse section (TS), contrast enhanced upper abdominal CT-Urograph of same patient, normal looking

kidneys, no cortical cysts or discernible synchronous contrast-enhanced tumor; C, Coronal view, abdominopelvic contrast-enhanced CT-urography (15 minutes post-contrast delayed films) of the patient showing mild calyceal dilatation of the left kidney upper pole minor calyx and the upper moiety of the middle pole minor calyx; D, The lower left ureter(or lower right ureter) does not demonstrate lower ureteric obstruction.

Investigations done on her revealed the following:- Urinalysis/ Chlamydial antigen tests: Her urine was clear amber, pH 5.0, specific gravity 1.015, glucose, protein, nitrite, ketones and bilirubin were negative, yeast cell epithelial cell (x). There was no leucocyturia; she had candiduria; urine culture yielded moderate growth of candida albicans. A repeat urinalysis, urine culture yielded no significant growth of Candida albicans. This followed initial treatments at the FMC with no resolution of symptoms-including loin pains. Chlamydial antigens test was negative for Chlamydia trachomatis IgG and IgM antibodies. Serum electrolyte / creatinine level were as follows Na^+ 136 mmol/L, K 3.9, H_{CO_3} - 29.0 and urea 2.1 creatinine was 65mmol/L. Fasting blood glucose was 5.2 mmol/L. Her full blood count had the following results; Hemoglobin 12.6g/dl, WBC Total 6.7 $x10^9$/Litre, and platelet count $253x10^9$/L. Erythrocyte Sedimentation Rate (ESR) was 32mm/first hour [Westergreen]. WBC differential counts-neutrophil, 39%; lymphocytes, 41%; monocytes 07%; and eosinophils 13%. Ultrasound findings [abdominopelvic ultrasonography]- Kidneys of normal sizes (Right 10.7cm x 3.7cm; Left 9.8cm x 44cm) position and echotexture with good cortico-medullary differentiation. There was upper pole calyceal dilatation. No cysts or calculi were seen. Abdomino-pelvic Ultrasound Scan Findings: - Phleboliths in the abdominal pelvis; normal outline and wall thickness of the urinary bladder. Both kidneys were normal in position and size, right and 10.8cm, left 9.4 cm in their longitudinal dimensions. There was fullness of the upper moiety of the left calyceal system. Abdomino-pelvic CTScan: Both kidneys were found normal in position and size (Rt 10.8cm, Lt 9.4cm) outline and function. There was fullness of the upper moiety of the left calyceal system.No cyst, calculi or mass was seen in the renal system. All other findings were normal. CT diagnosis was mild left upper calicosis of unknown cause. We made a presumptive diagnosis of grade 2 kidney tuberculosis. The patient received multiple antibiotic therapies both at the referral hospital and at UPTH with no success. She is doing well on anti-tuberculous therapy.

4. Discussion

UPTH is a referral center for TB and most infective, communicable and non-communicable diseases in the Niger Delta Region of South- Southern Nigeria. Data presented here therefore reflects the situation in a large population of Southern Nigerians. The finding of nine (9) patients with UGTB within 17 years of team practice (hospital incidence of 25/100,000 patients' population) in this setting seems to suggest the rarity of the disease of this variant of TB infection in the Port Harcourt/Niger Delta environment where TB is generally considered endemic. What appears more realistic is that UGTB may actually be more common in the area than we observed in this study. However, this finding is high and worrisome for TB which is a contagious disease. This study also brings to the fore the challenges to be addressed in the development of an institutional, community or national management policy or protocol for prevention, diagnosis and treatment of UGTB in this region.

The observed difficulties, which are further elaborated herein, include challenges in tissue/ bacteriological diagnosis, dearth of data on the disease, challenges in early diagnosis, masking effects of more common diseases, lack of reliable screening tests that have high and acceptable levels of sensitivity, specificity and reliability, a seemingly low level of clinical suspicion among clinicians. However different reports on EGTB including UGTB in the literature indicate that this trend may be fairly global [8].

4.1. Relevant Pathology

The organisms that usually invade the urogenital tract in UGTB are Mycobacterium tuberculosis (MTB) and Mycobacterium bovis, and the route of infection is initially usually haematogenous from some primary infective focus or foci [9]. Sexual transmission occurs but appears generally less well studied [10]. We did not include reports on this route and TB of the female genital tract (FGTB) in this report.

The tuberculous organisms invade and multiplies in tissues of the urogenital tract and/or its associated organs with resultant host cell-mediated immune responses [11]. Dissemination of mycobacteria to kidneys/adrenals, epididymis and the prostate gland are usually haematogenous, to the testes commonly from the ipsilateral epididymis, while TB infections of the ureters and urinary bladder are usually extensions of KTB [12]. Seminal vesicles may be involved by direct luminal spread from any of the ipsilateral vas deferens, ejaculatory duct, testis and epididymis [13]. Direct spread of the infective organisms may occur from any involved contiguous tissues.

4.2. Classification

Proper classification/ grading of UGTB is necessary to determine treatment options as well as requirements for organs or systems support. Ekaterina Kulchavenya **[**14] [15] made a classification/staging of the disease (reproduced below) which we found a useful guide for its management.

Grading and Classification of type KTB and urinary tract TB (UTTB) (Ekaterina Kulchavenya [15] [14] (Kulchavenya 2009 -2010)

4.2.1 Urinary Tuberculosis [Utb]

"Kidney Tuberculosis [KTB] or Nephrotuberculosis)

- **Stage 1,** TB of the kidney parenchyma, (non-destructive form) is subject to conservative therapy.
- **Stage 2:** TB papillitis, Small-destructive form, is subject to conservative therapy, reconstructive surgery is indicated for complications only.
- **Stage 3**: Cavernous KTB, Destructive form, Recovery without surgery is rare.
- **Stage 4:** Polycavernous KTB, widespread destructive form, recovery with anti-TB drugs only is impossible; surgery is necessary, basically nephrectomy

4.2.2 Urinary Bladder Tb (Btb) [16]:

- **Stage 1**- tubercle infiltrative;
- **Stage 2-** erosive ulcerous;
- **Stage 3** – spastic cystitis (bladder contraction, false micro cystitis), in fact over active bladder;
- **Stage 4** – renal micro cystitis up to full obliteration

4.2.3 Classification of Male Genital Tuberculosis (Mgtb) [16]:

- **Stage 1**-TB epididymitis (unilateral or bilateral);
- **Stage 2**-TB orchiepididymitis (unilateral or bilateral)**;**
- **Stage 3**-Prostate TB (infiltrative or cavernous forms);
- **Stage 4-**TB of seminal vesicles**; 5**-TB of the penis"

4.3. Risk factors

Recrudescence of previously dormant infective TB foci and host immune dysfunction have been variously reported in the literature as the main mechanisms of evolution of EPTB, including UGTB. Documented risk factors associated with UGTB include stasis of urine, congenital malformations, traumatic / inflammatory lesions or instrumentation of the urogenital tract, intravesical immunotherapy with BCG, immunopaenia, organ transplantation, HIV / AIDS, urinary tract infection, urethral stricture disease and tumors of the urogenital tract[17]. These would be compounded by risk factors for transmission of MTb in endemic communities[18]. However, Ogbo FA et al [3] observed that alcohol use, smoking and diabetes mellitus were the most common risk factors for TB in HIV-negative Nigerians. Alcohol use [19,20], cigarette- smoking [21], hyperglycaemia and tissue insulin deficiency have been documented in the literature to cause immune dysfunction which is apparently germane to the recrudescence of active TB infection from hitherto dormant *in vivo* TB focus or foci [22, 23]. A risk factor that was common to 8 of 9 patients in this study was frequent contact with crowds of people, or working in overcrowded environments. They did this as lecturer, student or physical market traders respectively. That five out of nine patients with UGTB were from the local universities, even with the small sample size, is worrisome and should warrant an investigation into the sanitary conditions of these high institutions, and a study of the prevalence of PTB and UGTB in them.

The non-specific nature of clinical features and the available laboratory investigations in UGTB observed in this study agree with findings made by others in different previous studies [24, 25]. Loin (lumbar) pains, weight loss, lumbar mass, anorexia, anaemia, and the pathological anatomical changes of renal *enlarg*ement, cyst formation, hydrocalicosis, hydro nephrosis, pyonephrosis, and nephrolithiasis detected on imaging studies were features of late disease. However, that biochemical renal function test results were still within normal reference ranges for all the patients with KTB at these advanced stages of the disease, suggests that appropriate renal function imaging studies should be done(apart from testing for differential diagnoses) even if biochemical renal function tests are normal, when evaluating patients with UGTB. The acute on set of fever, pyrexia of 38^{o}C, chills, tachycardia, tachypnoea and renal angle tenderness observed in

Patient No. 2 were features of superimposed acute nontuberculous pyelonephritis and concomitant systemic inflammatory response syndrome (SIRS). This resolved with appropriate antibiotic therapy, based on antimicrobial susceptibility testing. However, the presence of these acute symptoms and signs may sometimes signal the synchronous TB at another site in the body, or may at times be paraneoplastic features of synchronous renal cell carcinoma [26].

In male genital TB [MGTB], scrotal swelling and testicular/ epididymal mass were presenting features of the two male patients with TB epididymitis (EPDTB). Careful clinical assessment and an index of suspicion were necessary to differentiate these lesions as EPDTB from chlamydial infections and the more common acute or chronic nontuberculous epididymo-orchitis which frequently complicates urethral instrumentation or prolonged urethral catheterization in our environment. This finding however corroborates the observations that painful or painless testicular epididymal mass is a very common presenting feature of male genital TB (MGTB) in this environment [27]. These epididymal lesions need to be well evaluated at first presentation. Lower urinary tract symptoms reported by these two patients were not primary symptoms of EPDTB but most likely were complications of prostatic involvement and chronic cystitis.

Patient No 8 is a quintessence of the tortuous paths of chronic severe morbidity with recurrent acute exacerbations requiring invasive surgeries that occurs with undiagnosed, untreated chronic abdominal tuberculosis. She further presented recently with bilateral hydronephrosis and bilateral nephrolithiasis. A combination of positive tests and her current favourable responses to anti tuberculous treatment is suggestive of TB infection. She is having supportive treatment, including correction of malnutrition and anaemia, to enable her withstand the metabolic responses to further major surgery. We consider that this patient may have extensive intra and retroperitoneal fibrosis. She is doing well on supportive treatment and preoperative anti-tuberculous chemotherapy.

4.4. Challenges in Diagnosis / Limitations of this study

The limitations of this study include lack of confirmatory histopathological and bacteriological diagnosis of most cases. Reasons for these limitations include [i] non-confirmatory nature of available diagnostic tests for UGTB and lack of intraoperative frozen section facilities. The available Gene Expert MTB/RIF System, had some inherent and local drawbacks in our setting, despite its reported advantages over mycobacterial culture, smear tests for acid and alcohol fast bacilli (AAFB), histopathology for TB granulomas and tuberculin tests in diagnosis of UGTB [28]. We therefore relied substantially on index of suspicion to make diagnosis. Clinical suspicion alone has its shortcomings which include incorrect diagnosis, unnecessary TB treatment with burden of side effects of drugs when incorrect diagnosis is made, complications of untreated disease if the disease is not treated early or not treated at all because of absence of definitive diagnosis [29][30]. To minimize the error margin of presumption in diagnosis, after evaluation of each case, we based diagnosis on a combination of clinical judgement and the following :-((i) positive results of Gene Expert Ultra System which works by polymerase chain reaction (PCR) (in one case),(ii) positive Mantoux tests, which we based on the Guidelines of the American Thoracic Society (ATS) and Centres for Disease Control and Prevention (CDC) [31]. (iii) presence of significant leuococyturia and significant sterile pyuria without other discernible causes.(iv) findings on intravenous urography (IVU), Ultrasound findings, CT Scan, CT-Urography and smear tests, (v) nature of pus on drainage or at surgery.(vi) raised erythrocyte sedimentation rate [ESR, Westergreen] which occurred on 8 of 9 patients.(vii) intra-operative findings and (viii) favourable responses to presumptive anti-tuberculous chemotherapy.

4.5. Surgical Intervention

The aims of surgical intervention in KTB patients operated, all of who presented with advanced TB, (Grades III and IV, vide supra), were preservation and restoration of organ function, and excision of bulky grossly infected and devitalized/ dead tissues. We believe this strategy also improved drug penetration of affected tissues. Preliminary nephrostomy and nephrolithotomy became necessary in one patient for drainage of pus and re-establishment of flow of urine. We ensured careful attention and timely removal of drains, and indwelling catheters to prevent persistent sinuses and fistulas. When there were cystic cavities, we found it better to marsupialize the cysts as opposed to incision and drainage alone. For instance, Patient No. 3 had a previous renal exploration in which the cysts were only incised with drainage of pus in another hospital but the cysts recurred with more complications and symptoms. In view of difficulties of confirmatory diagnosis, after counselling, we obtained broad consents for renal exploration from patients and their consenting relatives. We ensured scrupulous supportive treatment including correction of anaemia and malnutrition. Careful intra-operative observations and decision-making became crucial, and involved identification of extent of renal damage, residual renal tissues free of macroscopic disease, evidence-based decisions for or against partial nephrectomy, nephrectomy or reconstructive renal surgery.

Exclusion of common intra-operative macroscopic features of renal malignancy was essential for appropriate diagnosis and treatment. These, for the more common renal cell carcinoma (RCC), include enlargement of affected part of the kidney or the whole organ, golden-yellow or tan appearance, and pseudo capsule of compressed friable

parenchymatous tissues, and multiple or single complex cysts and /or areas of tissue necrosis [32]. Others include presence of prominent vessels (often flattened by large tumors) which course on the surfaces of the tumor due to neovascularization, covered by thin film of fibrous tissues and fat. Often multiple perforators communicate with the vessels. These perforators usually cause brisk bleeding during dissection and usually require swift control.

4.5.1 Lithotomy

Lithotomy is an important part intra-operative management of advanced UGTB. Calculi in the urinary tract [UT], apart from causing obstruction to urine flow and obstructive uropathy, may form reservoirs of pathogenic bacteria including mycobacteria. The pathogens may be harbored between the layers of the stone structure or form biofilms on stone surfaces. Bacterial biofilms and urinary tract calculi have been associated with increased bacterial resistance to many antimicrobials [33, 34, and 35]. Urolithiasis may therefore cause persistent, recurrent or unresolved urinary tract TB [UTB], even with adequate anti-tuberculous therapy. Calculi, especially spiky ones, may also cause urothelial abrasions and ulceration with resultant intravasation of infective materials and miliary TB. Similarly, calculi within the epididymis, vasa differentia and ejaculatory ducts of the male genital tract [MGT], may cause obstructive azoospermia, infertility and other complications.

5. Conclusion/ Recommendations

UGTB is common in the Niger Delta of Nigeria but confirmatory diagnostic tests with high sensitivity and specificity are lacking. Patients presented late with high disease burden and often required surgical intervention. A combination of high index of suspicion with confirmatory and non-confirmatory tests for TB are the currently available tools for diagnosis of UGTB. In KTB all cysts are drained of pus and marsupialized during surgery. All calculi are removed with minimal tissue damage. Timely removal of all devitalized tissues, drains, and stents should be ensured to limit spread of TB and prevent fistula formation. Exclusion of malignancy which may coexist with TB, and evaluation of residual organ function are important. Diagnosis and treatment of UGTB may improve in the region with (i) the development of early diagnostic/ screening test(S) for the disease (ii) minimizing delays by affected patients in reporting to medical facilities for treatment (ii) prompt diagnosis and treatment of common comorbidities, complications of the disease, and superimposed infections.

Compliance with ethical standards

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Disclosure of conflict of interest

There is no conflict of interest.

Statement of ethical approval

The present research work does not contain any studies performed on animals/humans subjects by any of the authors.

Statement of informed consent

Informed consent was obtained from all individual participants included in the study.

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