



PROFILE OF GENITOURINARY TUBERCULOSIS OVER A PERIOD OF 5 YEARS – A SINGLE INSTITUTIONAL STUDY.

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ABSTRACT **BACKGROUND AND AIM-** Tuberculosis (TB) is the commonest worldwide cause of mortality from infectious diseases 1 with nine million new cases and two million fatalities per year 2. There has been a paucity of data on genitourinary tuberculosis and its profile. Genitourinary tuberculosis is the most common extra pulmonary site that can cause obstruction, strictures and destruction of the renal unit.

METHODS -252 patients presented to the Department of Urology at St Johns medical college and hospital, Bangalore, Karnataka between July 2011 and August 2016 and were studied in a prospective manner. Detailed history, clinical examination, urine examination and culture, AFB smear and culture, imaging studies, PCR and cystoscopy and biopsy whenever needed were done and noted for all the patients

RESULTS- Urine AFB was positive in 89%, most common presenting symptom was frequency – urgency -82 % and the most common radiological finding was hydronephrosis accounting to 20.63 %. All these patients were stented. Nonfunctional kidney was noted in 8 patients for whom a nephrectomy was done, bladder augmentation was done in 4 patients, ureteroureterostomy and Boari flap in 2 patients for ureteric strictures. All surgical interventions were done after minimum 4 weeks of ATT. Almost all patients had symptom relief by 6 months of ATT.

CONCLUSION- Renal tuberculosis is a disease that must be kept in mind when a patient comes to us with unrelieved symptoms even after treatment or nonspecific symptoms especially with a background of tuberculosis in the past or family history of tuberculosis. The disease has a wide spectrum of presentation ranging from loin pain to nonfunctional kidneys. With early institution of therapy, both the cost and duration of treatment can be minimized.

KEYWORDS : GUTB, Renal tuberculosis, AFB smear / culture, stricture, hydronephrosis

INTRODUCTION

Tuberculosis (TB) is the commonest worldwide cause of mortality from infectious diseases ¹with nine million new cases and two million fatalities per year ² India alone accounts for nearly one third of global tuberculosis burden. A relative increase in extra-pulmonary TB has been reported due to a significant decline in pulmonary tuberculosis (PTB) and an only modest decline in extra-pulmonary TB ³. The genitourinary tract is a primary target of hematogenous infections ⁴ and is the most common site of extra-pulmonary TB⁵, comprising 14-41% of the same ^{6, 7}. Usually it is from silent bacilleamia accompanying pulmonary tuberculosis. However, these lesions in the kidney may not manifest clinically for years together ⁸.

Usually these patients have been treated and evaluated extensively by physicians at times and are referred to the urologist for unexplained symptoms or they can present late in the course of the disease when a complication develops. These cases can remain silent for a long time and cause irreversible destruction and nephron loss. However, when identified early it may be completely curable ⁹.

There has been a paucity of data on profile of genitourinary tuberculosis – its presentation, management and complications. It has been discussed extensively across various forums and a consensus on the diagnosis and management of genitourinary tuberculosis was made and approved by the Association of Southern Urologists on 12th July 2015. Our study emphasizes and defines the profile of genitourinary tuberculosis (GU TB) and the need to keep this diagnosis in mind while treating patients with chronic nonspecific urinary symptoms for early diagnosis and institution of treatment. This article aims at bringing out the vivid forms of presentation of GU TB, its course, complications and management.

MATERIALS AND METHODS

252 patients were referred to or presented primarily to the Department of Urology at St Johns medical college and hospital, Bangalore, Karnataka between July 2011 and August 2016 and were studied in a prospective manner. Ours being a tertiary care referral center, patients are referred to us from various states across the country and across the borders as well. We have treated patients presenting to us with

genitourinary tuberculosis from West Bengal, Bangladesh, Sri Lanka from among a few countries to mention. The majority of the patients who presented to us had been treated outside earlier and were referred here for persisting symptoms.

A detailed history and physical examination including past and family history of tuberculosis were noted. Chronic urinary symptoms like urgency not responding to conventional measures, recurrent or unresolved urinary tract infection (UTI) and constitutional symptoms like fever were recorded. A urine routine microscopy and culture as well as a chest x ray were done for all the patients. Urine acid fast bacillus (AFB) smear and AFB culture was sent for all patients. At least 3 early morning urine samples were analyzed. A bacterial load of 5000 organisms/ml is needed for a positive smear. In patients with increased frequency, at least 8 hours of collection of urine is needed for urine AFB. Sterile containers were collected from the lab and handed over to the patient for the same. All the patients were evaluated with a computed tomography scan (CT SCAN) / intravenous pyelography. Patients who had renal failure only a plain CT scan was done. Routine blood investigations were done. DMSA / DTPA scan was done as and when needed to confirm presence of a nonfunctional kidney / outflow obstruction. When urine AFB was negative, but imaging strongly suggestive of renal tuberculosis, urine PCR was done. Cystoscopy and biopsy was done for patients in whom AFB (smear and culture) was negative. A positive AFB smear with a radiological suspicion of renal tuberculosis was taken as a presumptive diagnosis while AFB culture was taken as a definitive diagnosis and so was the histology whenever available. Before starting ATT therapy, liver function test, Hemoglobin, Platelet count, ESR, renal function test (RFT), serum electrolytes and calcium were done at baseline and repeated at 1,2,4 and 6 months and as need arises. Urine AFB, culture +/- PCR were repeated at 2 months, if positive second line therapy was started. Patients were followed up for at least one year post treatment, with an advice to follow up yearly for the initial few years to detect development of late complications.

RESULTS

A total of 252 patients were diagnosed to have renal tuberculosis between July 2011 and August 2016 at St Johns Medical College and

hospital, Bangalore, India. There were 143 male patients (57%) and 109 female patients (43%) between the age group of 18 to 72 years. The average duration of symptoms varied from 3 months to 3 years.

The majority of the patients who presented to us had been treated outside earlier and were referred here for no symptomatic relief. The most common symptom in our study was frequency-urgency seen in 82% of patients followed by dysuria seen in 60% patients. The next most common symptom was fever seen in 40%. Out of these 100 odd patients who presented to us with fever it was noted that almost 80% patients had some other form of tuberculosis as well, the most common being pulmonary. Approximately 66 patients accounting to 26% presented with loin pain. Out of these 66 patients who presented with loin pain, 52 patients (20.6%) had hydronephrosis and 8 were found to have a nonfunctional kidney. The symptomatology of our patients was as in table 1.

Majority of the patients (82%) had sterile pyuria. Urine AFB samples were positive in 89% patients. For patients in whom renal tuberculosis was strongly suspected and urine AFB was negative, PCR was done. Urine PCR was positive in 18 out of 28 patients who were AFB negative. In the remaining, a biopsy defined the disease and cleared the dilemma.

Cystoscopy and biopsy was done for 10 patients that showed caseating granulomas suggestive of tuberculosis.

Radiologically about 52 patients had hydronephrosis accounting to 20.63%. Distortion/cavitation/scarring were noted in 46 patients accounting to 18.2%. Calcification was seen in 8.7% accounting to 22 patients. A nonfunctional kidney was seen in 8 patients and thimble bladder in 6 patients accounting to 3 and 2.3% respectively. (Table 2)

All the patients who had hydronephrosis on Computed tomography / IVP were taken up for RGP and stenting. All these patients were stented. About 8 patients who had no contrast excretion on CT/IVP were evaluated with a Renogram and found to have a nonfunctional kidney hence a nephrectomy was performed. Out of the 6 patients who had thimble bladder, 4 underwent augmentation using ileum. Two patients with ureteric strictures underwent Boari flap and ureteroureterostomy. Four patients out of the eight who had a nonfunctional kidney had features of pyonephrosis and a percutaneous nephrostomy was placed initially followed by nephrectomy. Out of the patients who were stented earlier on repeat RGP after 3 months, 4 patients were found to have pelviureteric junction obstruction (PUJO) and a pyeloplasty was performed later on. (Table 3)

X ray chest revealed features of pulmonary tuberculosis (PTB) in 62 patients. Out of the 45 patients who had renal failure, renal functions normalized in 30 patients (11.9%), while the remaining 15 patients progressed to Chronic kidney disease. 6 patients eventually became dialysis dependent. Out of the 38 (15%) patients who had developed hypertension, blood pressures normalized in 30 patients (11.9%). Symptomatic relief of frequency-urgency, dysuria and hematuria was noted in almost all patients after a treatment of 6 months.

DISCUSSION

GUTB usually affects adults between the second and fourth decades of life and is reported as being rare in children.¹⁰ There is often a long latent period (5-40 years) between the original pulmonary infection and the appearance of clinical renal disease which explains why renal involvement is rare before the age of 20 years.¹¹ In our series there were 143 male patients (57%) and 109 female patients (43%) between the age group of 18 to 72 years. The mean age of presentation was 42 years. Nonspecific symptoms is the most common cause of this condition being missed by many practitioners. Voiding symptoms like frequency; dysuria;¹² pyuria;¹⁰ back, flank, or abdominal pain;¹³ and microscopic or macroscopic hematuria may be the presenting feature. Systemic symptoms of fever, weight loss, and anorexia are less common.^{10,13} In our study the most common presenting symptom was frequency-urgency in 82% patients followed by dysuria (60%). Constitutional symptoms such as fever, weight loss, night sweats may not always be present. When present they should raise a suspicion of coexisting pulmonary tuberculosis. Though fever is less common, 40% of our patients gave history of fever. This was one observation in our study which differed from other studies. Other causes of fever were ruled out in all these patients.

Hematuria and culture-negative pyuria may be seen at urine analysis. As per the consensus on the diagnosis and management of Genitourinary Tuberculosis by association of Southern Urologist on July 12th 2015, Urine AFB smear – at least 3 early morning urine samples should be analyzed. A bacterial load of 5000 organisms/ml is needed for positive smear. In case of increased day/night urinary frequency, at least 8 hours of collection of urine is required for AFB smear. Routine ZN staining has a sensitivity and specificity of 60-70% and 90-95% respectively. Auramine/Rhodamine staining with fluorescent microscopy increases sensitivity by 10-15% as compared to ZN staining. Smear positivity alone should not be considered as diagnostic of tuberculosis since chronic infections as non-tubercular mycobacteria (NTM) is not uncommon and do not usually respond to the conventional ATT. AFB culture by conventional LJ medium is still the gold standard and has a sensitivity and specificity of 80-85% and 98% respectively. The main drawback of this technique is that it requires 6-8 weeks for the results. Radiometric culture methods give results in 2-3 weeks and are equally sensitive (replaced by MGIT-mycobacterial growth indicator tube, nowadays). In our study a ZN staining-AFB smear and culture was done for all patients. Smears were positive in 89% patients. For patients in whom urine AFB was negative but imaging highly suspicious for renal tuberculosis PCR was done. The next investigation in line was cystoscopy and biopsy. 10 of our patients were diagnosed with tuberculosis by biopsy.

36.5% of patients with GUTB have a previous diagnosis of TB, or abnormal imaging studies.⁴ Evidence of active TB or an abnormal chest radiograph is present in around 50% of cases.¹¹ As per some studies only 20-30% of GUTB patients will have a previous history of PTB; an additional 25-50% will have radiographic evidence of prior subclinical PTB.¹⁴ In Our study, a total of 80 patients had other forms of tuberculosis. All of them had presented with fever as one of their complaints if not the chief complaint. Out of the 80, 62 had active or healed lesions of pulmonary tuberculosis.

Renal tuberculosis should be suspected and treatment may be initiated if the tubercle bacillus is identified microscopically in a urine specimen.¹³ The definitive diagnosis requires culture of tubercle bacillus from the urine and 90% of affected patients could have a positive culture.¹⁵ However, in our study, a positive culture was obtained only in 106 patients accounting to 42%. Negative urine cultures are possible in cases where cavitory lesions are sealed off.⁹

Most of our patients were referred to us in view of non-resolving symptoms and had taken treatment at other places. Many had come with an IVU done already. In a series of 45 patients, the IVU pointed to the diagnosis of urinary TB in 88%.¹⁶ However, approximately 10-15% of patients who present with active renal TB may have normal urography findings.¹⁷ Isolated parenchymal miliary tubercles usually produce urographic findings only when a calyx is involved.¹⁸ The earliest urographic change occurs in the minor calyces, with subtle initial signs such as minimal calyceal dilatation¹⁹ and mild loss of calyceal sharpness due to mucosal edema.¹⁸ As the disease progresses, the calyceal outline becomes more irregular, fuzzy, and ragged and, later, feathery and moth-eaten in appearance. The various abnormalities of the intravenous urograms associated with genitourinary tuberculosis are impaired excretion of contrast, renal parenchymal calcification, cavitation and fibrosis, infundibular stenosis and calyceal dilation, ureteral stricture and hydronephrosis and non-complaint contracted bladder. The various radiological abnormalities noted in our patients are listed in table 2.

CT is useful both in the diagnosis of renal TB and in assessing its severity in terms of loss of renal function and involvement of other organs in the abdomen.²⁰ Barring very early changes, most findings on an IVU should be detectable on CTU carried out on current high-end MDCT scanners. CT, in general, shows more details of pathologic anatomy due to the availability of axial images for review and is superior to retrograde pyelography (RGP), IVU, and USG in detecting multiple small urothelial lesions.²¹ However, until such time as it is proven to be superior to IVU in assessing early renal TB changes, the IVU shall reign supreme. RGP is reserved for patients with renal failure, drug allergy, or patients with metal implants that might cause artifacts. In one patient, the entire kidney was calcified and had formed a putty kidney (figure 1 – CT IMAGE). This patient underwent nephrectomy. 10% of our patients had normal imaging.

As per the consensus by the southern urologists, the criteria for

definitive diagnosis of tuberculosis is as follows - One major and/or two minor criteria are required for definitive diagnosis of Tuberculosis.

Major Criteria

- a) Granulomatous lesion in biopsy specimen
- b) AFB in urine or tissue (smear or culture)
- c) Positive PCR

Minor Criteria

- a) IVU/CT/MRI findings suggestive of GUTB
- b) Hematuria
- c) Raised ESR
- d) Pulmonary changes of old Koch's

82 % of our patients had raised ESR. Once a diagnosis of GUTB was made these patients were started on ATT with baseline LFT (liver function test). Short course chemotherapy for 6 months was given which included 2 months of initial intense treatment phase with 4 drugs followed by 4 months of continuation treatment phase with 2 drugs. Surgery or steroid therapy by itself was no indication to prolong ATT. ATT was given on empty stomach since food, antacids containing aluminum and magnesium and prokinetics reduces the absorption of the medicines significantly. When not tolerated, the medication was given 2 hours after breakfast or 2-3 hours after dinner. Pyridoxine supplementation was given to all patients. Urine AFB smear and culture and PCR were obtained at 2 months, after the completion of the initial intensive regimen of therapy. If positive, second line therapy was considered.

52 of our patients had obstructed drainage patterns and needed RGP and ureteral stenting accounting to 20.6 %. The indications for stenting include to maintain drainage during medical therapy, post-surgery to facilitate drainage and healing and post dilatation of ureteral strictures. These patients were kept on ureteral stents till strictures had stabilized. Each time a stent was removed RGP was done to look at the clearance of contrast and if need be, patient was re stented. When the stents were removed patient was advised to follow up with an IVU or DTPA after 1 to 3 months .The patients in whom ureteral stenting is not possible percutaneous nephrostomy should be done. Infundibular stenosis with calyceal dilatation and abscess drainage were other indications. On follow up, 4 patients had developed pelviureteric strictures and pyeloplasty was done for them. Another patient developed an isolated mid ureteric stricture for whom an ureteroureterostomy was performed. Boari flap was performed for another patient who had developed a lower ureteric stricture. Eight patients underwent nephrectomy for nonfunctional kidney. Nephrectomy may also be done for hypertension due to tuberculous nephropathy and co existing renal cell carcinoma. Eight patients had a thimble bladder for which four underwent augmentation cystoplasty using ileum while the other two were not willing for any surgical intervention when the possibility of lifelong CIC (clean intermittent catheterization) was explained to them. Two of these patients are on second year follow up now and are doing well. Stents were removed on an average after 14 months varying between 6 to 36 months.

To conclude, renal tuberculosis is a disease that must be kept in mind when a patient comes to us with unrelieved symptoms even after treatment or nonspecific symptoms especially with a background of tuberculosis in the past or family history of tuberculosis. Patients having negative urine cultures, abnormal urine analysis and localizing urinary symptoms should also be looked upon with a high degree of suspicion. Urine AFB smear, AFB culture and IVU are handy in diagnosing tuberculosis. Urine PCR and cystoscopy – biopsy are the next diagnosing modalities. The prevalence of renal tuberculosis is under reported as a large number of cases are either missed or not reported. With early institution of therapy, both the cost and duration of treatment can be minimized.

TABLE 1: SYMPTOMATOLOGY OF OUR PATIENTS

symptom	No of patients	percentage
Frequency and urgency	206	82
Dysuria	151	60
Fever	100	40
Loin pain	66	26
Hematuria	55	22
Hypertension	38	15
Renal failure	45	18

TABLE 2: RADIOLOGICAL PROFILE OF OUR PATIENTS

Radiological finding	No of patients	Percentage
Distortion , cavitation , scarring	46	18.2
Hydroureteronephrosis	52	20.63
Calcification	22	8.7
Nonfunctional kidney	8	3
Thimble bladder	6	2.3
Urolithiasis	20	7.9

TABLE 3: SURGICAL PROFILE OF OUR PATIENTS

Surgery	No of patients	Percentage
Ureteral stenting	52	20.6 %
Nephrectomy	8	3.1 %
Augmentation	4	1.58%
Boari flap	1	0.39%
Ureteroureterostomy	1	0.39 %
Pyeloplasty	4	1.58%
Percutaneous nephrostomy	4	1.58 %



Figure 1: putty kidney

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