香港泌尿外科學會
Hong Kong Urological Association

Abstract no.: PR 1-16

30TH ANNUAL SCIENTIFIC MEETING 2025

A literature review investigating the epidemiology, treatment, and outcomes of urinary tract fungal bezoars caused by *Aspergillus* species

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Background: Urinary tract infections (UTIs) have a rising impact on public health. In 2019, there were 404.6 million new UTI cases and led to 236,790 deaths. Fungal UTIs, once rare, are increasing due to more immunocompromised patients. In particular, urinary tract fungal balls, also known as mycetoma and fungal bezoars, represent a challenging and potentially serious condition characterized by the formation of fungal masses within the urinary tract. The diagnosis of urinary tract fungal ball infections could be difficult and delayed due to the non-specific clinical manifestations and overlapping symptoms with other urinary tract conditions. While *Candida* species have been described, there is insufficient knowledge on *Aspergillus* species. This study reviews the current evidence and answers the knowledge gap on the epidemiology, presentation, diagnostic methods, and treatment options of urinary tract fungal balls caused by *Aspergillus* species.

Methods: A literature search using PubMed, MEDLINE (OVID) and EMBASE (OVID) databases was conducted to identify relevant literature from the inception of each electronic database to August 16, 2024, with additional studies from reference searching. Studies were screened for eligibility and relevant information was extracted. A risk of bias assessment using the JBI Critical Appraisal Checklist for Case Reports was performed. Data was synthesized qualitatively.

Results: 25 case reports were included. Nearly all (n=24, 96.0%) patients had underlying risk factors. The most common underlying conditions were diabetes mellitus (n=13, 52.0%) and receiving immunosuppressant treatment (n=9, 36.0%). The most common symptoms were non-specific, including flank pain (n=17, 68.0%) and oliguria (n=15, 60.0%). 3 (12.0%) patients were initially misdiagnosed. 23 (92.0%) recovered and treatments mainly combined surgical and antifungal approaches.

Conclusions: More research is warranted to inform best clinical practice as the current evidence mainly consists of case reports. Clinical guidelines shall be developed, and clinicians shall maintain high vigilance on this disease.

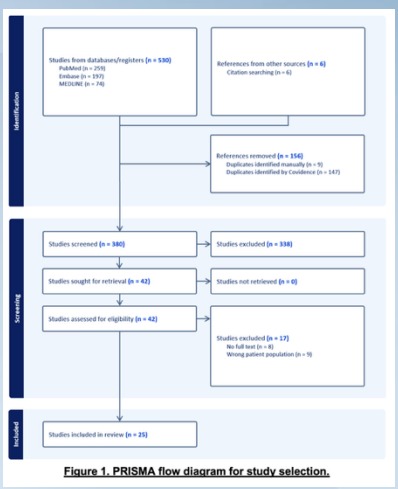

Figure 1. PRISMA flow diagram for study selection.

Author year	Age (years) /	predisposing factors	Presenting signs and symptoms	Diagnostic method	Aspergillus species	Surgical treatment	Antifungal treatment	Outcome
Ahuja 20 09 [13]	48/ F	diabetes	flank pain, rectal urinary tract infections, passage of small particles during urination	urine culture, microbiological examination of fungal balls	not mentioned	Ureteroscopic removal	oral itraconazole; amphotericin B irrigation through ureteral catheter	Recovered
Bibler 1987 [14]	34/ M	diabetes	flank pain	Histopathological examination of fungal mass, ureteral stent insertion, histopathological examination of fungal ball passed	flavus	Ureteral stent insertion	Intravenous amphotericin B; oral fluconazole	Recovered
Campbell 1992 [15]	63/ M	Chronic obstructive pulmonary disease, corticosteroids, antibiotics, bladder catheter	pain, hematuria, fever, chills	Microscopic exam, immunofluorescent staining, fungal culture, resection	fumigatus	Transurethral prostatic resection	Intravenous amphotericin B	Recovered
Choi 2011 [16]	56/ M	Diabetes, alcoholic liver cirrhosis	flank pain, fever, chills	histological examination of mass obtained from ureteroscopy	not mentioned	Ureteroscopic removal	Refused antifungal treatment, given amphotericin B on 2nd presentation	Died of sepsis and hepatorenal syndrome
Comings 1962 [17]	27/ F	Diabetes, Addison's disease, congenital abnormalities	Flank pain, vomiting, weakness, haematuria, suprapubic pain on voiding	Culture of renal cast obtained from nephrectomy	fumigatus	Nephrectomy	None	Recovered
Dervisoglu 20 08 [18]	70/ M	diabetes	nausea, vomiting, gait disorder	Histological examination of mass obtained from bladder wall biopsy	not mentioned	Percutaneous nephrostomy	Intravenous caspofungin,	Recovered
Gulelius 199 8 [19]	30/ M	renal transplant recipient, corticosteroid, immunosuppressive drugs,	anuria	Histological examination of mass obtained from cystoscopy	not mentioned	Ureteral stenting, percutaneous nephrostomy, ureteroscopic removal	amphotericin B irrigation through bladder catheter, oral itraconazole	Recovered
Haq 20 07 [20]	45/ M	Diabetes, previous ureteroscopy with intracorporeal pneumatic lithotripsy (ICPL) and ureteric stenting	Flank pain, fever, dysuria, passing gwhitish mass urine	Histological examination of mass passed in urine	fumigatus	none	Intravenous amphotericin B, oral itraconazole	Recovered
Kalantari 20 17 [21]	18/ M	pre-Bacute lymphoblastic leukaemia, on induction therapy	flank pain, anuria	Histological examination of mass obtained from ureteroscopy	not mentioned	Percutaneous nephrostomy, haemodialysis, ureteral stenting, ureteroscopic removal	amphotericin B irrigation through nephrostomy tube s, oral voriconazole	Recovered
Kamel 2 003 [22]	63/ F	kidney transplant recipient, cortical osteoid, immunosuppressive drugs	Flank pain, oliguria	Urine culture	not mentioned	percutaneous nephrostomy, limited polar nephrectomy	Intravenous amphotericin B, amphotericin B irrigation through nephrostomy tube, oral itraconazole	Recovered
Kishnani 2 009 [23]	60/ M	none	anuria	Histological examination of mass obtained from ureteroscopy	fumigatus	percutaneous nephrostomy, ureteral stenting	Intravenous amphotericin B, oral itraconazole	Recovered
Kuet er 200 2 [11]	40/ M	diabetes, history of drug abuse	flank pain, nausea, vomiting, terminal dysuria, haematuria, anuria	Histological examination of mass obtained from cystoscopy	flavus	Ureteral stenting, cystoscopic removal	Oral Ifluconazole, intravenous amphotericin B	Recovered
Lee 20 10 [24]	72/ F	non-functioning gleft kidney, history of chronic renal failure	flank pain, fever, nausea, vomiting, decreased urine output	Origin allymisdiagnose d as urinary calculi, histological examination of mass obtained from pyelotomy	not mentioned	percutaneous nephrostomy, removal by pyelotomy	itraconazole	Recovered
Ludwig 2005 [25]	50/ M	History of alcohol abuse	urinary retention, abscessed epididymoorchitis	Histological examination of resected prostate, midstream urine culture	fumigatus	transurethral prostate resection, suprapubic catheter, sacrotomy, nephrectomy	Intravenous caspofungin, intravenous voriconazole	Recovered
Nain 20 13 [26]	58/ M	Diabetes, hypertension, urinary stenting	flank pain, difficulty in passing urine, fever, nausea, vomiting, decreased urine output	Origin allymisdiagnose d as urinary calculi, histological examination of mass obtained from ureteroscopy	flavus	Ureteroscopic removal	voriconazole	Recovered
Najaf i2 013 [27]	45/ M	Diabetes, previous urinary stenting, antibiotics	flank pain, occasional dysuria, passing whitish soft mass	Origin allymisdiagnose d as a remnant of urinary calculi and bacterial infection, histological examination of mass obtained from ureteroscopy, confirmed by pyomyelosechain reaction	terreus	Ureteral stenting, ureteroscopic removal	oral itraconazole, oral voriconazole	Recovered
Perez-Arellano 200 1 [29]	34/ M	Previous urinary stenting	Flank pain, oliguria, irritative voiding, fever	Culture of urine sample sfrom nephrostomy and midstream urine	flavus	percutaneous nephrostomy	Oral Ivoriconazole	Recovered
Paul 201 3 [28]	38/ M	diabetes, intravenous drug user	Low back pain	Urine culture and histological examination of mass sspassed in urine	flavus	none	Oral Itraconazole	Recovered
Sadagah 201 7[30]	29/ M	kidney transplant recipient, cortical osteoid, immunosuppressive drugs	decreased urine output, passing white materials, haematuria, flank pain	Urine culture and histological examination of biopsyof transplanted kidney	fumigatus	Haemodialysis, nephrectomy of transplanted kidney	Oral Ivoriconazole	Recovered
Shamin 202 0 [31]	37/ F	diabetes, hypertension	Flank pain, urinary retention, passage of white mass	histological examination of mass passed in urine	not mentioned	none	Refused amphotericin B, given oral itraconazole and oral Ivoriconazole	Recovered
Smaldone 20 06 [32]	50/ F	diabetes	Flank pain, nausea, vomiting, fever, chills, decreased urine output, haematuria	Urine culture from percutaneous nephrostomy and histological examination of mass obtained from ureteroscopy	flavus	percutaneous nephrostomy, ureteroscopic removal	Intravenous voriconazole	Recovered
Ullah 2016 [33]	55/ F	diabetes, hypertension	Flank pain, fever, burning micturition	urine culture, microbiological examination of fungal mass adhered to ureteral stent	not mentioned	Ureteral stenting, percutaneous nephrostomy	Intravenous amphotericin B, oral itraconazole	Recovered
Vuruskan 20 05 [34]	51/ M	renal transplant recipient, urinary stent, corticosteroid, immunosuppressive drugs	decreased urine output, dyspnoea, fever	Histological examination of mass obtained from cystoscopy	not mentioned	Ureteronecystostomy, ureteral stenting, dialysis	Amphotericin B	Died of acute circulatory failure, ischemia, disseminated infection
Yoon 20 10 [35]	60/ F	Chronic obstructive pulmonary disease, antibiotics, corticosteroids, bronchiectasis with sputum culture positive for Aspergillus	flank pain, abdominal distension, reduced urine output, haematuria	Histological examination of fluid from percutaneous nephrostomy tube	nidulans	Haemodialysis, percutaneous nephrostomy	Intravenous amphotericin B, oral voriconazole	Recovered
Zhu 2011 [36]	46/ M	hepatitis B liver cirrhosis, liver transplant recipient, corticosteroid, immunosuppressive drugs	cough, dyspnoea, fever, low back pain	histological examination of mass passed in urine	flavus	none	amphotericin B colloidal dispersion, intravenous and oral itraconazole	Recovered