

Urological Manifestations in HIV and AIDS: At Tertiary Referral Centre

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ABSTRACT

Introduction: The prevalence of HIV and AIDS continues to grow worldwide. Urological manifestations of HIV and AIDS such as urolithiasis, obstructive uropathy, complicated UTI and malignancy are often first clinical signs. With the availability of antiretroviral drugs and surgical intervention, the prognosis of HIV-infected patients is same as that of general population.

Aim: To evaluate incidence of urological manifestations, their treatment and outcome in HIV and AIDS patients.

Material and Methods: This was retrospective study conducted at Institute of Nephro-Urology, Bengaluru from June 2011 to May 2016. Inclusion criteria were all HIV and AIDS patients suffering from urological diseases. The data were collected in a Microsoft® Excel database and analysed through SPSS 20 version.

Results: A total of 161 patients (male -93, female-68) with HIV and AIDS were analysed retrospectively. The most common presentations were Urosepsis (31.05%), Urolithiasis (27.32%), Malignancy (16.77%), Renal dysfunction (11.18%), Stricture urethra (7.45%), GUTB (Genito-Urinary Tuberculosis) (3.10%) and others (2.4%). The most common surgical intervention done was DJ stenting. Renal abscess, psoas abscess and stricture urethra patients underwent surgical intervention. Uncomplicated UTI was treated conservatively. Sepsis and pyogenic infections were more common in patients with CD4 count <200 cells/mm³. Out come was compared with non HIV-AIDS patients.

Conclusion: Complicated UTI followed by calculus disease were most common in our study. It is important to create awareness of the urologic manifestations of HIV and AIDS among the retroviral positive patients.

Keywords: CD4 count, DJ stenting, Highly active antiretroviral therapy

INTRODUCTION

HIV is a retrovirus that replicates rapidly and kills helper T cells, which are the body's main cellular defense against infection [1,2]. HIV spreads through contact with blood, semen and cerebrospinal fluid. Low concentrations are found in tears, saliva, breast milk, urine and cervical and vaginal secretions. HIV virus has also been isolated from brain tissue, lymph nodes, bone marrow cells and skin [3,4]. Both viral load and CD4 T-cell count are reliably used to monitor and prognosticate disease progression to AIDS.

Many studies have revealed that Urologic complications like renal dysfunction, urinary tract infection, urogenital tuberculosis, prostatitis, prostatic abscess, epididymo-orchitis, urologic malignancies, sexual dysfunction and infertility are often the first clinical signs of HIV and AIDS [5-9]. With Highly Active Antiretroviral Therapy (HAART) and antibiotic prophylaxis, HIV positive patients have a life expectancy of >20 years [10].

Now with longer survival to an almost normal life expectancy, there is an increase in the prevalence of HIV-related disorders, including urological problems that arise relating to infections, malignancies or drug treatment [11-13]. These patients with common urologic disorders are now actively treated for quality of life. Thus the population living with HIV, needs treatment for expected age related conditions, complications of the disease and therapies they receive and therefore, the need of the awareness of the urologic manifestations of HIV and AIDS arises and advising these patients for the subsequent management of the respective disorders is good for both the patient and the Urologists.

This study was designed to evaluate the incidence of urological manifestations in HIV and AIDS patients and various treatment modalities with outcomes. To evaluate incidence of urological

manifestations, their treatment and outcomes in HIV and AIDS patients.

MATERIALS AND METHODS

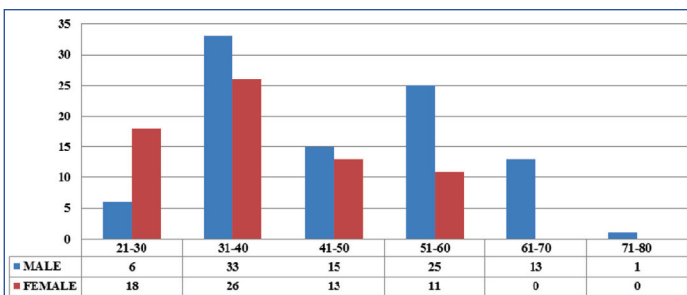
This retrospective study was conducted in the department of urology, Institute of Nephro-Urology, Bengaluru, Karnataka, India from June 2011 to May 2016. The data were collected in a Microsoft® Excel database from the hospital records and analysed through SPSS 20 version.

Inclusion criteria: Patients with urological and nephrological manifestations, newly diagnosed HIV Positive and already on HAART were included and their treatment modality and treatment outcome were assessed.

Exclusion criteria: Negative HIV and AIDS cases. The institutional ethical committee approval was obtained for the study.

RESULTS

From 2011 to 2016 total institutional admissions were 20922, out of these 161 (0.77%) patients were retroviral positive. Among these 93 (57.8%) were male and 68 (42.2%) were female. Prevalence was more in the age group of 31-40 years i.e., 59 patients (36.6%) followed by 36 patients (22.4%) in the 51-60 years age group [Table/Fig-1]. In total 57(35.4%) patients were newly detected retroviral positive on admission and 104(64.6%) patients were retroviral positive already taking HAART with mean duration varying between 3 to 6 years and mean CD₄ count varied between <100 to >400mm³ [Table/Fig-2]. In 28 (17.4%) patients duration of retroviral disease was 4-5 years followed by 5-6years in 18 (11.2%) patients and one patient was retroviral positive since 10 years [Table/Fig-3,4].



[Table/Fig-1]: Graph showing prevalence of retroviral positive cases among age groups.

Manifestations	New retroviral positive cases on admission	Already on HAART	Mean duration of HAART (Yrs)	Mean CD4 count per mm ³	HAART regimen
Urosepsis	16	34	3.8	<100	3TC+NVP+ZDV
Urolithiasis	17	27	6	>400	3TC+NVP+ZDV
Malignancy	9	18	3.6	<200	3TC+NVP+ZDV
Renal Dysfunction	11	7	5.5	<150	3TC+NVP+ZDV
Genito urinary tuberculosis	-	6	3	<100	EFV+3TC+TDF
Others	4	12	3	<200	3TC+NVP+ZDV

[Table/Fig-2]: Showing various urological manifestations, duration of HAART, mean CD4 count and HAART regimen.

Others- Stricture urethra, Voiding dysfunction and Amyloidosis. HAART-Highly active anti-retroviral therapy, 3TC-Lamivudine, NVP-Nevirapine, ZDV-Zidovudine, EFV-Efavirenz, TDF-Tenofovir

Sex	Positive on admission(New cases)	Total
Male	35	57
Female	22	

[Table/Fig-3]: Showing total number of HIV positive cases (Newly detected) on admission.

Urological Manifestations

Among 161 retroviral positive cases, most common manifestation was Urosepsis 31% followed by Urolithiasis 27.3%, Malignancy 16.77%, Renal dysfunction 11.18%, Genito-urinary tuberculosis 3.72% and others which include Stricture urethra 7.45%, Voiding dysfunction 1.86% and Amyloidosis 0.62% of cases.

Urosepsis

Out of 161 retroviral positive cases 50 cases manifested with urosepsis among which 16 cases were retroviral positive on admission to hospital and 34 were already on HAART. The most common mode of presentation was pyelonephritis in 18 cases followed by urinary tract infections-15. The common clinical presentation was fever with chills, pain abdomen and hypotension. Mean CD₄ count was <100 cells/mm³. On investigations total count was increased and E.Coli was the most common organism isolated on urine culture followed by candida, mixed aerobic and anaerobic growth and no growth in some cases. A total of 28 patients were treated conservatively and 22 patients underwent conventional surgical treatment as per general population with standard theatre precaution during surgery. Mean hospital stay varied between 3 days to 10 days with no mortality [Table/Fig-5].

Duration (yrs)of HAART in retroviral positive (old cases-AIDS)	0-1Y	1-2Y	2-3Y	3-4Y	4-5Y	5-6Y	6-7Y	7-8Y	8-9Y	9-10Y	Total
Male	7	9	6	3	16	11	2	2	1	1	104
Female	5	7	4	5	12	7	2	4	0	0	

[Table/Fig-4]: Showing duration of HAAART (in years) in already diagnosed retroviral positive cases (old cases-AIDS) on admission.

Manifestation	Number of cases	Intervention	Mean hospital stay (days)
Pyelonephritis	18	DJ stenting-8	5
		Conservative-10	6
UTI	15	Conservative	3
Psoas Abscess	5	Incision & Drainage	5
Renal Abscess	4	Incision & Drainage	8
Epididymorchitis	3	Conservative	4
Fournier Gangrene	2	Debridement	10
Prostatic Abscess	1	TUIP	7
Testicular Abscess	1	Orchiectomy	3
Periurethral Abscess	1	Incision & Drainage	4

[Table/Fig-5]: Showing various intervention in Urosepsis and hospital stay DJ stent-Double J stent, TUIP-Trans urethral incision of prostate.

Incidence of calculus	Ureteric calculus	Renal calculus	Vesical calculus
Male	17	7	4
Female	13	3	0

[Table/Fig-6]: Urolithiasis in retroviral cases.

Manifestation	No.of cases	Intervention	Mean hospital stay (days)
Urolithiasis	44	URSL+ DJ stenting- 21	3
		DJ- 9	4
		PCNL- 5	5
		PCN- 4	3
		Cystolithotomy- 2	4
		Cystolitholapaxy- 2	2
		Pyelolithotomy- 1	7

[Table/Fig-7]: Various interventions done in urolithiasis patients and hospital stay URSL-Ureteroscopic Lithotripsy, DJ stent-Double J stent, PCNL-percutaneous nephrolithotomy, PCN-percutaneous nephrostomy.

Urolithiasis

A total of 44 Retroviral positive cases had urolithiasis. Seventeen cases were newly diagnosed HIV positive on admission and 27 cases were already on HAART. Thirty cases had ureteric calculus and renal and vesical calculus were present in 10 and 4 cases respectively [Table/Fig-6]. The most common clinical presentation was abdominal pain in 28 cases followed by pain and fever in 5 cases. Mean CD₄ count was >400 cells/mm³. Patients with urosepsis underwent surgical intervention after control of sepsis. All patients with urolithiasis underwent surgical procedures with standard operation theatre precautions with mean hospital stay varying between 2 days to 7 days with no mortality [Table/Fig-7]. Most calculi on evaluation were Calcium Oxalate.

Malignancies

A total of 27 cases had malignancy with Carcinoma Cervix as most common manifestation in 13 cases followed by Carcinoma Bladder-8. Most common clinical presentation was Obstructive Uropathy in 15 cases. Mean CD₄ count was <200 cells/mm³. All cases underwent surgical intervention with hospital stay between 2 days to 8 days with nil mortality. The final histopathological reports after surgery were transitional cell carcinoma in carcinoma bladder, squamous cell carcinoma in carcinoma penis, cervix and vagina

Malignancy	Carcinoma bladder	Carcinoma penis	Renal cell carcinoma	Carcinoma cervix	Carcinoma vagina
Male	6	3	1	0	0
Female	2	0	0	13	2

[Table/Fig-8]: Incidence of malignancies in retroviral cases.

Manifestations	No. of cases	Intervention	Mean hospital stay(days)
Carcinoma bladder	8	TURBT	6
Carcinoma penis	3	Partial Penectomy	3
Renal cell carcinoma	1	Radical Nephrectomy	8
Carcinoma cervix	13	DJ Stenting	2
Carcinoma vagina	2	DJ Stenting	2

[Table/Fig-9]: Surgical interventions done in malignancies and hospital stay
TURBT-Trans urethral resection of bladder tumour, DJ stent-Double J stent

and clear cell renal cell carcinoma in renal cell carcinoma [Table/Fig-8,9].

Renal Dysfunction

Among 18 Patients with renal dysfunction on dialysis, 11 cases were retroviral positive on admission and seven were already on HAART with mean duration of HAART 5.5 years. Mean CD₄ count was <150 cells/mm³. All of them referred from nephrology for vascular access. Renal biopsy showed Nephritis. All patients underwent arterio-venous fistula creation under strict theatre precautions with one day hospital stay.

Genito-Urinary Tuberculosis

Six cases had genito-urinary tuberculosis. Out of which five cases presenting as obstructive uropathy underwent DJ stenting and one case had tubercular testis treated by simple Orchiectomy [Table/Fig-10]. Two cases in obstructive uropathy had active pulmonary tuberculosis as sputum examination showed AFB positive. Mean CD₄ count was < 100cells/mm³ and mean hospital stay was six days with no mortality.

Other Manifestations

Among 16 patients, four were detected retroviral positive on admission and 12 were already on HAART with mean duration of HAART was three years. Mean CD₄ count was <200 cells/mm³. They clinically presented with dysuria, thinning and reduced urinary stream and increased urinary frequency. On radiological evaluation, diagnosed to have stricture urethra. Eight cases underwent direct visual internal urethrotomy as stricture was short segment, thin with less spongiofibrosis on palpation, present at proximal bulbar urethra. Three cases under went buccal mucosal graft urethroplasty for long segment anterior urethral stricture and in one case staged urethroplasty was done for pan anterior urethral stricture. Mean hospital stay varied from 5 days to 10 days. Three patients had

Manifestations	Ureteric stricture	Testis
Male	2	1
Female	3	0

[Table/Fig-10]: Genitourinary tuberculosis manifestations.

Manifestations	No. of cases	Intervention	Mean hospital stay (days)
Stricture urethra	12	DVIU- 8 BMG Urethroplasty- 3 Staged Urethroplasty- 1	4 10 5
Voiding dysfunction	3	UDS	2
Amyloidosis	1	TURBT	5

[Table/Fig-11]: Surgical interventions done in other manifestations and hospital stay
DVIU-Direct Visual Internal Urethrotomy, BMG-Buccal Mucosal Graft, UDS-Urodynamic Study, TURBT-Trans Urethral Resection of Prostate

Manifestations	HIV-AIDS patients	Mean hospital stay (days)	Non HIV-AIDS patients	Mean hospital stay(days)
Urosepsis	50	5.5	50	6
Urolithiasis	44	3	680	4
Malignancy	27	2	170	2
Renal Dysfunction	18	1	2500	1
Genito urinary tuberculosis	6	6	110	7
Stricture urethra	16	6.3	550	7

[Table/Fig-12]: Mean hospital stay of HIV-AIDS and non HIV-AIDS patients

Manifestations	Our Study	Mean CD4 count (cells/cumm)	Other studies	Mean CD4 count (cells/cumm)
UROSEPSIS				
Pyelonephritis	11.18%	<100	19.35% [26]	100
UTI	9.3%		17% [27]	<500
UROLITHIASIS	27.32%	>400	5-22% [28]	300
MALIGNANCY				
Ca.cx	8.0%(n=13/161),	<200	14.1% (n=20/141) [29]	257
Ca.bladder	4.9% (n=8/161)		3.8% (n=1/26)	
penile cancer	1.86%(n=3/161)		7.6% (n=2/26)	
RENAL DYSFUNCTION	11.18%	<150	15.5% (n=192/1239) [30]	200
GUTB	3.10%	<100	12.5% [31]	150
STRICTURE URETHRA	7.45%	<200	37.5% [32]	<400

[Table/Fig-13]: Urological manifestations in other studies with respect to our study [25-31]

voiding dysfunction with sterile urine underwent urodynamic study and found to have overactive bladder treated with anti-cholinergic. One patient underwent TURBT for bladder growth presenting clinically as hematuria. Histopathological examination reported as amyloidosis and hospital stay was five days [Table/Fig-11].

Between June 2011 and May 2016, a total of 4060 non HIV-AIDS patients were admitted with similar urological manifestations as that of HIV-AIDS positive patients in our study. These patients underwent treatment modality for respective urological disease similar to HIV-AIDS patients without mortality and there mean hospital stay was same as that of HIV-AIDS patients [Table/Fig-12].

DISCUSSION

Urologic disorders are often the first clinical signs that indicate possible HIV infection [4].

In our study the most common presentation was urosepsis in 50 cases of the study population. The most common mode of presentation is pyelonephritis in 18 cases followed by UTI in 15 cases and the mean CD4 count is <100 cells/mm³. On urine culture Escherichia coli was the most common organism isolated followed by candida, mixed aerobic and anaerobic growth and no growth in some case. Twenty eight patients were treated conservatively and 22 patients underwent conventional surgical procedures as per general population with standard theatre precautions during surgery. The result of this finding was in consonance with a similar study carried out in Calaber, Nigeria which recorded a prevalence of 25.3% [14] while a much higher prevalence of UTI 48.7% was recorded in South Africa [15]. These findings agreed that UTIs are higher in retroviral positive individuals than retroviral negative individuals with CD4 count <200 cells/mm³ with Escherichia coli as the most common isolated organism [15].

In our study 104 (64.6%) patients were taking HAART-regimen (3TC+NVP+ZDV) with mean duration of treatment four years. A 57(35.4%) patients were newly diagnosed on screening and referred to ART center. In the present study the incidence of urolithiasis was

7.32% with calcium oxalate being the most common on stone analysis. According to Hoffmann C and Mulcahy F, and Meraviglia P et al., Indinavir caused urolithiasis in 5–25% of HIV positive patients treated with the drug [16,17]. In the present study non of the drugs of HAART regimen are known to cause crystaluria and stone formation [18].

In patients with HIV on HAART there has been an increase in the incidence of non-AAMs (AIDS-Associated Malignancies) including anal cancer, lung cancer, hepatocellular carcinoma, vaginal cancer, leukemia, oropharyngeal cancer, colorectal cancer, penile cancer, and renal cancer [19-23]. In our study the most common malignancy was carcinoma cervix 13 (19.11%) followed by carcinoma bladder 8(8.6%).

Renal dysfunction in patients with HIV can be caused by nephrotoxic medications such as antibiotics and antifungals, metabolic dysfunction and volume depletion as a result of chronic diarrhea, urethral obstruction from malignancy, infections, and intrinsic diseases such as HIV-Associated Nephropathy (HIVAN), which occurs in 10–30% of patients with HIV [24]. In our study, 18 (11.18%) patients were referred from nephrology for vascular access. Renal biopsy showed Nephritis.

Hospital stay was similar to that of general population admitted with similar manifestations as that of HIV and AIDS patients during the study period [Table/Fig-13] [25-31]. Coelho LE et al., have shown that the length of hospital stay in AIDS related and non-AIDS related events is almost similar [32].

CONCLUSIONS

In our study, urosepsis is the most commonest presentation followed by urolithiasis with CD4 count between <100 cells/mm³ and CD 4 >400 cells/mm³ respectively. With timely diagnosis and prompt treatment of urological disorders, the outcome and prognosis is same as that of general population.

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