## **ORIGINAL RESEARCH**

with HIV on antiretroviral therapy: prevalence, influencing factors, and quality-of-life implications

Investigating bothersome lower urinary

tract symptoms among people living

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### Abstract

Background Urological complications are not uncommon among people living with HIV and are often the initial clinical manifestation of HIV and AIDS. These complications, when presenting with bothersome lower urinary tract symptoms (LUTS), can significantly impact the Quality of life (QoL) of affected individuals. We, therefore, conducted a study aiming at determining the prevalence of bothersome LUTS, identifying factors influencing the severity of these symptoms, and examining their influence on the QoL among people living with HIV on antiretroviral treatment (ART).

Methods A cross-sectional study was conducted among randomly selected adult HIV-positive patients who attended the Care and Treatment Center at Muhimbili National Hospital, located in Dar es Salaam, Tanzania, from September 2021 to February 2022. Data was collected using a guestionnaire that incorporated the American version of the International Prostate Symptom Score (IPSS). The IPSS was utilized to assess the severity of LUTS and their influence on the QoL. Descriptive statistics were used to summarize the results, and ordinal regression analysis was employed to assess the factors influencing the severity of LUTS.

Results The prevalence of LUTS in the study population was 57.8%, with mild symptoms (mean IPSS 3.92 ± 1.92) being the most common manifestation. The mean age of the study participants who presented with LUTS was 47.89 ± 12.05 years, and the majority were females (55.6%). Factors that were significantly associated with increased severity of LUTS included male sex (OR 2.75; 95% CI 1.59–4.75; p < 0.001), age above 49 years (OR 3.02; 95% CI 1.49–6.16; p = 0.002), ART use for over 10 years (OR 3.03; 95% CI 0.9–6.10; p = 0.021), and HIV stage IV (OR 2.42; 95% CI 0.9–3.4; p=0.047). The majority of the study participants reported an above-average QoL, with only 9.7% of them reporting unhappy-terrible experiences with urinary symptoms. However, a statistically significant (p < 0.001) inverse correlation between QoL and the severity of LUTS was observed.

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**Conclusions** In light of these findings, policymakers and healthcare providers should integrate routine assessment and management of LUTS into the care protocols tailored for these high-risk groups. This proactive approach holds the potential to enhance the QoL and overall welfare of people living with HIV.

**Keywords** Acquired immunodeficiency syndrome, Antiretroviral treatment, Highly active antiretroviral therapy, Human immunodeficiency virus, International Prostate Symptom Score, Lower urinary tract symptoms, Quality of life

#### 1 Background

Human immunodeficiency virus (HIV) infection continues to be a significant global public health concern. Approximately 25.7 million individuals live with HIV in Africa where one-third of all new global cases are reported, underscoring the disproportionate burden of the disease [1]. However, with the advent of highly active antiretroviral therapy (HAART), the prognosis of HIV infection has shifted from being a terminal condition to a manageable chronic illness, particularly for those who have access to treatment. Around 64% of individuals affected by HIV in Africa have access to HAART, marking a notable milestone in combating the disease [1]. However, in the context of Tanzania, 5% of adults aged 15 to 64 years are affected by HIV, with only 52% of them achieving viral load suppression, rendering the problem a major health concern in the index and comparable settings [2].

Urological complications are not common among people living with HIV and are often the initial clinical manifestation of HIV and acquired immunodeficiency syndrome (AIDS) [3]. Several factors increase the likelihood of developing lower urinary tract symptoms (LUTS) in these individuals; some of which include an increased incidence of urinary tract infections, sequelae of opportunistic infections, and the direct effect of the virus on the central and peripheral nervous systems [4, 5]. Moreover, urologic complications are also attributed to adverse effects of antiretroviral medications such as Indinavir which has been linked to the development of urolithiasis [6]. Such complications presenting with bothersome LUTS can therefore have a significant impact on the quality of life (QoL) in this cohort of patients [7].

Considering the limited availability of data on the topic, we conducted a study to explore the prevalence of bothersome LUTS, identify factors influencing the severity of these symptoms, and examine their influence on the QoL among HIV-positive individuals on HAART. The study findings will contribute to a better understanding of the burden of the problem and facilitate the development of targeted holistic interventions aiming at improving the QoL of people living with HIV.

#### 2 Methods

#### 2.1 Study design and area

A cross-sectional study was conducted at Tanzania's National Hospital located in Dar es Salaam from September 2021 to February 2022. The hospital encompasses an HIV Care and Treatment Center (CTC) that was established in 2004. The CTC runs 5 clinic days during a regular working week, attending an average of approximately 50 patients per day. In alignment with national treatment guidelines, the hospital offers comprehensive access to all available antiretroviral treatments (ARTs) to effectively manage HIV patients.

#### 2.2 Study participants

The study population consisted of HIV-positive individuals who attended the CTC clinics at Muhimbili National Hospital between September 2021 and February 2022. We included adults aged 18 years or older who had been on a single antiretroviral therapy (ART) regimen for a minimum of 6 months. However, certain patients were excluded from the study, including those requiring immediate admission, individuals with urethral or suprapubic catheters, and patients with a previous or current medical or surgical history of a urological condition(s) known to significantly impact LUTS (i.e., benign prostatic hyperplasia, prostatic surgeries, etc.). Study participants were selected using a systematic random sampling technique. Two clinic days were randomly chosen using a lottery method, and individuals attending the clinic on those specific days were systematically sampled.

#### 2.3 Sample size

To determine the minimum required sample size for the study, the Cochrane 1977 formula for cross-sectional studies was utilized [8]. The calculations employed a standard normal deviation at a 95% confidence interval (Z=1.96), a proportion of the problem of interest within the population of 37.3% (P=0.373) [9], and the margin of the standard error of 5% (e=0.05). Substituting these values into the formula yielded an estimated minimum sample size of 250 participants. Considering an anticipated

response rate of 90%, the adjusted sample size was determined to be 280 participants.

#### 2.4 Assessment of the severity of lower urinary tract symptoms

In this study, we utilized the International Prostate Symptom Score (IPSS) developed by Barry et al. in grading the severity of LUTS [10]. The word "Prostate" in the score is a misnomer since the score has been used to evaluate LUTS in non-prostatic conditions regardless of gender. The IPSS comprises 7 graded questions that pertain to voiding symptoms. A score ranging from 0 to 7 indicates mild symptoms, 8–19 indicates moderate symptoms and 20–35 indicates severe symptoms. The American version of the score incorporates an 8th question on QoL that was also evaluated in this study [11]. To ensure accurate data collection from participants who were not fluent in English, we primarily utilized the recently validated Swahili version of the IPSS [12].

#### 2.5 Data collection

This study utilized a pre-tested questionnaire that integrated the American version of the IPSS. The questionnaire was designed to gather demographic data, information on the severity of LUTS, data on the ART regimen and treatment duration, HIV immunological status (CD4 count and viral load), and the HIV clinical stage based on the World Health Organization (WHO) classification. Additionally, the questionnaire also captured information on the QoL of the participants.

#### 2.6 Data management and analysis

The data analysis was performed using IBM<sup>®</sup> SPSS<sup>®</sup> Statistics version 23. Descriptive statistics were employed to summarize the results. To assess the factors influencing the severity of LUTS, ordinal regression analysis was utilized, with severe LUTS as the reference category. The association between the QoL and the severity of LUTS was examined using the chi-square test. The analysis was conducted at a 95% confidence interval (CI), and a p-value less than 0.05 was considered statistically significant.

#### 2.7 Ethical considerations

The study received ethical approval from the Institutional Review Board of Muhimbili University of Health and Allied Sciences. Before their participation, written informed consent was obtained from all participants. The study was performed in accordance with the ethical standards laid by the 1964 Helsinki Declaration and its later amendments on comparable ethical standards.

#### **3 Results**

#### 3.1 Prevalence of lower urinary tract symptoms

Within the study population, the prevalence of LUTS was recorded at 57.8%, where the predominant manifestation was mild symptoms (mean IPSS  $3.92 \pm 1.92$ ) (Fig. 1; Table 1). It is worth noting that after establishing the prevalence of LUTS, the ensuing analysis focused exclusively on 279 participants who presented with these symptoms.

#### 3.2 Sociodemographic and Clinical characteristics of participants with lower urinary tract symptoms

Table 2 summarizes the sociodemographic and clinical characteristics of the 279 study participants who were found to have LUTS. The mean age of study participants was  $47.89 \pm 12.05$  years, and the majority were females (55.6%). Half of the participants (50.5%) presented with a CD4 count of  $\geq$  500 cells/mm<sup>3</sup>. Notably, an undetectable viral load was observed in 81% of the participants, and only 16.8% of all participants were found to have HIV stage IV. The most commonly prescribed treatment regimen was Tenofovir, Lamivudine, and Dolutegravir (TLD) (87.5%), with a significant proportion (53.4%) of participants receiving ART treatment for over 10 years. Furthermore, severe LUTS tended to occur at a significantly higher proportion among males, individuals of advanced age, those with prolonged ART use, and those with higher HIV stages.

## 3.3 Factors influencing the severity of lower urinary tract symptoms among the study participants

Table 3 presents a summary of the results from the ordinal regression analysis of the factors influencing the severity of LUTS. Significant associations (p < 0.05) with increased severity of symptoms were observed for several variables. These included male sex (OR 2.75; 95% CI 1.59–4.75; p < 0.001), age above 49 years (OR 3.02; 95% CI 1.49–6.16; p = 0.002), the use of ART for more than 10 years (OR 3.03; 95% CI 0.9–6.10; p = 0.021), and being categorized as HIV stage IV (OR 2.42; 95% CI 0.9–3.4; p = 0.047).



Fig. 1 Proportion of lower urinary tract symptoms among HIV-positive patients

Table 1	Severity	of lower	urinary	tract s	symptoms	(LUTS)	among
HIV-posit	ive patie	nts exper	riencing	LUTS			

Variable	Frequency	Mean IPSS	IPSS range
Overall	279	$7.48 \pm 5.75$	1-32
Mild LUTS	167	$3.92 \pm 1.92$	1-7
Moderate LUTS	97	$10.96 \pm 2.64$	8–19
Severe LUTS	15	$24.57 \pm 3.70$	20-32

LUTS lower urinary tract symptoms, IPSS International Prostate Symptom Score

#### 3.4 The Influence of lower urinary tract symptoms on the quality of life

Most of the study participants reported an above-average QoL, with only 9.7% of them reporting unhappy-terrible experiences with urinary symptoms. Nonetheless, a note-worthy statistically significant (p < 0.001) inverse correlation between QoL and the severity of LUTS was observed (Table 4; Fig. 2).

#### 4 Discussion

HIV status has been identified as an independent predictor of LUTS; however, previous studies have not definitively established the prevalence of these symptoms among individuals who are HIV-positive [13]. When compared to a similar socioeconomically and geographically matched general population [14], our study showed an approximately threefold higher prevalence of LUTS among individuals living with HIV (20.2% vs. 57.8%). Furthermore, prior studies have established a notably higher frequency of severe LUTS among HIV-positive individuals [13]; however, in our study, mild symptoms constituted the most prevalent presentation. These findings highlight the impact of HIV on the development of LUTS and its effect on symptom severity.

Our findings also revealed that more severe symptoms were observed among males and individuals of advanced age. Furthermore, a significant association with severe LUTS was observed among males, individuals aged 50 years or older, and those with HIV stage IV. Given the high prevalence of obstructive uropathies in these groups [15], undiagnosed urological conditions could account for these findings. Similar findings have also been reported in previous studies [16, 17], underscoring the influence of these factors on the severity of LUTS.

Severe symptoms also appeared to be more common among those with low CD4 counts, and high viral load.

Variable	Mild LUTS: n = 167 (%)	Moderate LUTS: n = 97 (%)	Severe LUTS: n = 15 (%)	Total: n = 279 (%)	p-value
Sex					
Male	58 (46.8)	55 (44.4)	11 (8.9)	124 (44.4)	< 0.001
Female	109 (70.3)	42 (27.1)	4 (2.6)	155 (55.6)	
Age groups (years)					
< 40	50 (72.5)	18 (26.1)	1 (1.4)	69 (24.7)	< 0.001
40-49	56 (70.9)	23 (29.1)	0 (0.0)	79 (28.3)	
>49	61 (46.6)	56 (42.7)	14 (10.7)	131 (47.0)	
Education level					
No formal	5 (41.7)	6 (50.0)	1 (8.3)	12 (4.3)	0.505
Primary	68 (59.7)	39 (34.2)	7 (6.1)	114 (40.9)	
Secondary	62 (66.0)	29 (30.8)	3 (3.2)	94 (33.7)	
College/University	32 (54.2)	23 (39.0)	4 (6.8)	59 (21.1)	
Marital status					
Married	82 (61.2)	44 (32.8)	8 (6.0)	134 (48.0)	0.770
Not married	85 (58.6)	53 (36.6)	7 (4.8)	145 (52.0)	
Employment status					
Formal	89 (54.3)	66 (40.2)	9 (5.5)	164 (58.8)	0.063
No formal	78 (67.8)	31 (27.0)	6 (5.2)	115 (41.2)	
CD4 count (cells/mm <sup>3</sup> )					
≤200	25 (58.1)	16 (37.2)	2 (4.7)	43 (15.4)	0.742
201–499	62 (65.3)	29 (30.5)	4(4.2)	95 (34.1)	
≥ 500	80 (56.7)	52 (36.9)	9 (6.4)	141 (50.5)	
Viral load (copies/mL)					
Undetectable	132 (58.4)	80 (35.4)	14 (6.2)	226 (81.0)	0.219
< 1000	5 (41.7)	7 (58.3)	0 (0.0)	12 (4.3)	
≥1000	30 (73.2)	10 (24.4)	1 (2.4)	41 (14.7)	
Antiretroviral therapy regimen					
TLD	147 (60.2)	84 (34.4)	13 (5.3)	244 (87.5)	0.546
TLE	4 (80.0)	1 (20.0)	0 (0.0)	5 (1.8)	
ALD	12 (60.2)	5 (26.3)	2 (10.5)	19 (6.8)	
ETA	3 (42.9)	4 (57.1)	0 (0.0)	7 (2.5)	
Others	1 (25.0)	3 (75.0)	0 (0.0)	4 (1.4)	
Antiretroviral therapy duration	of use (years)				
≤1	9 (81.8)	2 (18.2)	0 (0.0)	11(3.9)	0.036
>1 but≤10	82 (68.9)	33 (27.2)	4 (3.4)	119 (42.7)	
>10	76(51.0)	62 (42.6)	11 (7.4)	149 (53.4)	
HIV stage (WHO)					
Stage I	28 (66.7)	12 (28.5)	2 (4.8)	42 (15.1)	0.039
Stage II	58 (66.7)	28 (32.2)	1 (1.1)	87 (31.2)	
Stage III	62 (60.2)	35 (34.0)	6 (5.8)	103 (36.9)	
Stage IV	19 (40.4)	22 (46.8)	6 (12.8)	47 (16.8)	

Table 2 Socio-demographic and clinical characteristics of HIV-positive patients experiencing lower urinary tract symptoms

Bold: p < 0.005

ALD Abacavir, Lamivudine, Dolutegravir, ETA Emtricitabine, Tenofovir, Atazanavir, LUTS lower urinary tract symptoms, TLD Tenofovir, Lamivudine, Dolutegravir, TLE Tenofovir, Lamivudine, Efavirenz, WHO World Health Organization

Similar observations have been reported by Breyer et al., who suggested that a direct effect of the virus and/or HAART could be the contributing factors [13]. Building on Breyer's findings, it is well established that individuals with HIV/AIDS have a greater vulnerability to urinary tract infections and also experience neurological **Table 3** Factors influencing the severity of lower urinary tract

 symptoms among HIV-positive patients

Variable	Odds ratio (95% CI)	p-value
Sex		
Male	2.75 (1.59–4.75)	< 0.001
Female	Ref	-
Age group (years)		
>49	3.02 (1.49-6.16)	0.002
40-49	1.25 (0.56-2.83)	0.586
<40	Ref	_
Education level		
No formal	1.21 (0.3–4.51)	0.792
Primary	0.66 (0.22-1.29)	0.170
Secondary	0.53 (0.31-1.29)	0.180
College/University	Ref	-
Marital status		
Married	1.23 (0.72-2.09)	0.445
Not married	Ref	-
Employment status		
Formal	1.47 (0.85–2.58)	0.167
No formal	Ref	-
CD4 count (cells/mm <sup>3</sup> )		
≤200	1.04 (0.56-2.32)	0.885
201–499	0.71 (0.42-1.28)	0.268
≥500	Ref	-
Viral load (copies/mL)		
Undetectable	1.81 (0.75-4.41)	0.187
< 1000	2.39 (0.53–9.97)	0.252
≥1000	Ref	-
Antiretroviral therapy regimen		
TLD	1.29 (0.11–9.1)	0.781
TLE	1.52 (0.24-21.27)	0.847
ALD	1.41 (0.14–9.36)	0.941
ETA	0.79 (0.16-6.71)	0.778
Others	Ref	-
Antiretroviral Therapy duration	of use (years)	
>10	3.03 (0.9–6.1)	0.021
>1 but≤10	1.7 (0.3–3.54)	0.545
≤1	Ref	-
HIV stage (WHO)		
Stage IV	2.42 (0.9–3.4)	0.047
Stage III	1.01 (0.42–2.44)	0.980
Stage II	0.82 (0.34–1.99)	0.671
Stage I	Ref	-

Bold: p < 0.005

ALD Abacavir, Lamivudine, Dolutegravir, ETA Emtricitabine, Tenofovir, Atazanavir, TLD Tenofovir, Lamivudine, Dolutegravir, TLE Tenofovir, Lamivudine, Efavirenz, WHO World Health Organization complications such as bladder areflexia and hyporeflexia, which subsequently complicates into urinary stasis and eventual urinary tract infection [18]. Additionally, a significant positive association between severe LUTS and prolonged use of ARTs was observed in our study, similar to Breyer's suggestions. Nonetheless, the influence of ART treatment regimens on the severity of LUTS could not be established in our findings.

The association between the severity of LUTS and their impact on QoL has been evidenced in previous studies [19, 20], a trend that is reaffirmed in the present study. A clear shift of skewness from positive to negative was observed in the QoL assessment, corresponding to the increasing severity of LUTS. Several factors that could have contributed to this correlation include physical discomfort, psychological distress, sleep disruption, limitations in activities, strain on relationships, effects on sexual function, self-perception, and the burden of treatment. Nonetheless, additional studies are essential to validate these postulations.

The study presents certain limitations that warrant consideration. Firstly, the employed cross-sectional study design was unable to comprehensively capture the dynamic nature of the disease over time. Moreover, the influence of center-specific factors could impact the external validity of the findings, potentially limiting their generalization to a broader population of individuals living with HIV. Lastly, participants might have provided socially desirable responses, potentially affecting the accuracy of self-reported data.

#### 5 Conclusions

Our study findings have revealed a high prevalence of LUTS among adult individuals living with HIV. Factors that were found to be positively associated with the severity of LUTS included male sex, age above 49 years, the use of ART for more than 10 years, and HIV stage IV. Moreover, the study findings also demonstrated an association between more severe LUTS and poor QoL among the study participants.

In light of these findings, policymakers and healthcare providers should integrate routine assessment and management of LUTS into the care protocols tailored for these high-risk groups. This proactive approach has the potential to contribute to an enhanced QoL and the

QoL responses (IPSS)	Mild LUTS: n = 167 (%)	Moderate LUTS: n = 97 (%)	Severe LUTS: n = 15 (%)	Total: n = 279 (%)	p-value
Delighted	54 (32.3)	1 (1.0)	0 (0.0)	55 (19.7)	< 0.001
Pleased	44 (26.4)	7 (7.2)	0 (0.0)	51 (18.3)	
Mostly satisfied	48 (28.7)	19 (19.6)	1 (6.7)	68 (24.3)	
Mixed	14 (8.4)	32 (33.0)	0 (0.0)	46 (16.5)	
Mostly dissatisfied	4 (2.4)	23 (23.7)	5 (33.3)	32 (11.5)	
Unhappy	2 (1.2)	15 (15.5)	8 (53.3)	25 (9.0)	
Terrible	1 (0.6)	0 (0.0)	1 (6.7)	2 (0.7)	

#### Table 4 Influence of lower urinary tract symptoms on the quality of life among HIV-positive patients

IPSS International Prostate Symptom Score, LUTS lower urinary tract symptoms, QoL quality of life



Fig. 2 The relationship between the severity of lower urinary tract symptoms and quality of life among HIV-positive patients

overall well-being of people living with HIV. Nonetheless, future longitudinal and multicenter studies should be considered to access the dynamic nature of the disease and enhance the generalizability of findings to a broader spectrum of individuals living with HIV.

#### Abbreviations

ALD	Abacavir, Lamivudine, Dolutegravir
AIDS	Acquired immunodeficiency syndrome
ART	Antiretroviral treatment
CTC	Care and Treatment Center
ETA	Emtricitabine, Tenofovir, Atazanavir
HAART	Highly active antiretroviral therapy
HIV	Human immunodeficiency virus

- IPSS International Prostate Symptom Score
- LUTS Lower urinary tract symptoms
- QoL Quality of life

- TLD Tenofovir, Lamivudine, Dolutegravir
- TLE Tenofovir, Lamivudine, Efavirenz
- WHO World Health Organization

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#### Author contributions

Conception and Design: IHB, OVN, FAM, DWK, and AHM; Acquisition of Data: IHB; Analysis and Interpretation of Data: IHB, DWK, and AO; Drafting the Article: IHB, DWK, and AO; Critical Revision of Intellectual Content: OVN, FAM, DWK, and AHM. All authors read and approved the final manuscript.

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#### Availability of data and materials

The dataset is available from the corresponding author upon reasonable request.

#### Declarations

#### Ethics approval and consent to participate

The study received ethical approval from the Institutional Review Board of Muhimbili University of Health and Allied Sciences; Reference number: DA.282/298/01.C/. Written informed consent was obtained from all participants.

#### Consent for publication

Consent for publication was obtained from all participants.

#### **Competing interests**

The authors declare that they have no competing interests.

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