Original

Pattern of Sexually Transmitted Infection Cases at a Tertiary Health Facility in Rivers State, Nigeria: A Cross-Sectional Study

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ABSTRACT

Background: This study assessed the pattern of sexually transmitted infection (STI) cases at the sexual and reproductive health clinic in a tertiary health facility in Rivers State, Nigeria.

Methods: A cross-sectional study design was used to retrospectively review 502 patient records from January 2019 to December 2023. Data were collected through a structured extraction sheet and analysed using SPSS version 27, with descriptive statistics and Pearson's Chi-Square test.

Results: The median age of the respondents was 28 years, the range was 60 years, with the majority being single (342, 68.1%), males (263, 52.4%), and urban residents (397, 79.1%). The highest number of cases (115, 30.9%) occurred in 2019. Genital warts were the most common STI, affecting adolescents aged 10–19 (75, 33.3%), females (3, 50.0%), and those who were separated. Significant associations were found between STI patterns and age ($\chi^2 = 110.26$; p < 0.001), sex ($\chi^2 = 123.47$; p < 0.001), marital status ($\chi^2 = 61.47$; p < 0.005), and year of presentation ($\chi^2 = 93.85$; p < 0.001). HIV status ($\chi^2 = 38.32$; p < 0.004). and a previous history of STI ($\chi^2 = 28.53$; p < 0.054).

Conclusion: Genital warts are the most common STI; they disproportionately affect young people, while the older population experiences more fungal infections and herpes. Females were more likely to experience multiple STIs. The study recommends early sexual health education and HPV vaccination, especially among adolescents, to curb STI spread.

Keywords: Pattern, Sexually Transmitted Infections, cases, Health facility, Sexual, Rivers State



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INTRODUCTION

Sexually transmitted infections (STI) remain a significant public health concern globally, with varying prevalence and patterns observed across different regions. ^{1,2} Sexually transmitted infections can negatively impact the sexual and reproductive health of the reproductive age group. Sexually transmitted infections are a group of infectious diseases caused by viruses, bacteria, fungi, parasites, protozoa or arthropods that are generally acquired by sexual contact. It includes more than 30 different conditions, among which the most common are gonorrhoea, chlamydial infection, syphilis, trichomoniasis, chancroid, genital herpes, genital warts, human immunodeficiency virus and hepatitis B. ³

A study from India on the Patterns of STI in a tertiary care hospital showed that the majority (27.5%) of people diagnosed with STI had syphilis followed by condylomata accuminata (22.6%), urethral discharge syndrome (20.1%) and vaginal discharge syndrome (17%). Paudel et al. documented condyloma acuminata as the most common STI in their study. According to the World Health Organisation (WHO), sexually transmitted infections are one of the five types of disease for which adults around the world most commonly seek medical help.

Female adolescents and young women have the highest risk of curable STI globally.⁶ Studies indicate that the majority of STI cases are reported among individuals aged 22-44 years, with a higher incidence in females compared to males. ^{7,8} The syndromic approach is commonly used for diagnosis and treatment, which helps in managing infections effectively despite the challenges of limited resources.⁸

Africa has been inundated with limited availability and poor-quality health data. ⁹ In Nigeria, the burden of STI is exacerbated by factors such as restricted access to health care, inadequate sexual health education, and socioeconomic challenges. ¹⁰ According to the World Health Organisation (WHO), Nigeria experiences a high prevalence of STI, with significant variations between urban and rural areas. This disparity is evident in Rivers State, where tertiary health facilities serve as centres for diagnosing, treating, and managing STI. In Rivers State, Nigeria, there is a paucity of data on the pattern and prevalence of STI in this region, especially within tertiary health facilities that serve a broad and diverse population. Limited availability and poor quality of

health data have been shown to negatively impact digital health and evidence-based practice adversely. ¹¹

In Rivers State, Nigeria, the burden of STI is particularly pronounced, necessitating focused public health interventions and robust clinical responses. Tertiary health facilities, equipped with specialised resources and expertise, play a crucial role in managing and mitigating the impact of these infections.⁸. Rivers State, situated in the Niger Delta region, is characterised by its diverse population, high urbanization rate, and a dynamic socioeconomic environment. These factors contribute to the unique epidemiological profile of STI in the region.

The sexual and reproductive health clinic at the tertiary health facility in Rivers State provides an invaluable dataset for understanding the patterns of STI in the region. Previous studies have highlighted a range of STI prevalent in Nigeria, including gonorrhoea, syphilis, chlamydia, and HIV/AIDS. The clinic's records offer insights into the demographic characteristics of affected individuals, common presenting symptoms, and the efficacy of treatment regimens. Analysing the patterns of STI cases at this clinic can reveal trends in incidence rates, identify high-risk populations, and inform targeted public health strategies. Similarly, understanding local STI patterns can guide the allocation of resources, the design of educational campaigns, and the development of prevention programs tailored to the specific needs of the Rivers State population.

The STI clinic at the tertiary health facility in Rivers State offers a vital opportunity to study and address the patterns of STI in the region. By leveraging clinic data and existing research, healthcare providers can develop informed strategies to reduce STI incidence and transmission, improve patient outcomes, and ultimately enhance public health in Rivers State. The understanding of these patterns is essential for developing targeted interventions and policies to reduce the burden of STI in the region. ⁸ This study assessed the pattern of sexually transmitted infections among patients presenting at the Sexual and Reproductive Health Clinic in a tertiary health facility in Rivers State from 2019 to 2023.

Methods

Study area: The study was carried out at the STI clinic of the University of Port Harcourt Teaching Hospital. The hospital is a 950-bed health facility that offers tertiary



health care services, secondary and primary health care, due to the near collapse of the other facilities in the State and region. ¹².The sexual and reproductive health clinic is domiciled in the Department of Community Medicine, the endemic disease unit. The patients are from Port Harcourt and its environs and were recruited from the general outpatients' departments (GOPD), the accident and emergency unit, and the anti-retroviral clinic. The staffs include the Consultants, Residents, Nurses, and ward maids. Diagnosis is made from history, medical examination and laboratory.

Study design: The study used a cross-sectional design that retrospectively reviewed records of cases seen at the facility from January 1, 2019, to December 31, 2023. Study Population: All patients who presented to the clinic for the past 5 years were assessed through their case notes and relevant data abstracted.

Inclusion criteria: New and follow-up cases of patients seen at the sexual and reproductive health clinic of the University of Port Harcourt Teaching Hospital from January 1, 2019, to December 31, 2023. Exclusion Criteria: Cases of patients seen within the period with missing data were excluded.

Sample size: All cases of patients registered at the SRH clinic of the University of Port Harcourt Teaching Hospital from January 1, 2019, to December 31, 2023, that met the inclusion criteria were reviewed. Data will be obtained using data extraction sheets. The patients were clinically evaluated by a trained physician. The syndromes are cervical/vaginal discharge, genital ulcer disease herpetic, inguinal bubo, urethral discharge, lower abdominal pain, genital warts, and genital molluscum. Although all case files within the period were reviewed, for completeness' sake and also to serve as a guide to ensure the total population studied has a study population greater than the minimum sample size required and to demonstration that the number of cases available is statistically adequate to detect meaningful associations. The sample size was derived based on Cochran's formula for sample size calculation for a cross-sectional study, using an estimated prevalence of STI seen a of 18.2% ¹³ and providing for a further 10% allowance to compensate for incompletely filled case files. Sample size $n = \frac{Z^2 pq}{e^2}$. 14 Where n = Sample size to be obtained, Z = the normal curve, 1.96 at 95% Confidence Interval, e = margin of precision (5%), P =

18.2%, prevalence estimate of 18.2% 13 , q=1-p. A sample size estimate of 461 was used.

Sampling Technique: The total number of cases registered at the clinic within the period was reviewed. Study Instruments: Data were collected using a data extraction sheet, which has the socio-demographic and sexual activity and pattern of sexually transmitted infection sections:

Data Collection Methods/Data analysis: Data were collected by the author using a structured data extraction sheet designed for the study. Data analysis was done using IBM SPSS version 27. Descriptive statistics were used to summarise data. Pearson's Chi-square test was used to determine the association between outcome and independent variables. The level of statistical significance was set at $p \le 0.05$.

Ethical Considerations: Ethical approval was sought and obtained from the research and ethics committee of the University of Port Harcourt Teaching Hospital (UPTH/ ADM/90/S.11/VOL.XI/17010). Permission was obtained from the unit consultants. This study did not involve direct dealing with human subjects and therefore there was no need for consent from participants, no risk or threat to life.

RESULTS

Table 1: Socio-demographic characteristics of cases seen at the Sexual and Reproductive Health clinic from 2019 to 2023.

Characteristics	Frequency	Percentage
	No. n=502	(%)
Age group		
10-19	45	9.0
20-29	230	45.8
30-39	140	27.9
40-49	55	11.0
50-59	26	5.2
60-69	4	0.8
70-79	2	0.4
Sex		
Female	239	47.6
Male	263	52.4
Marital Status		
Divorced	5	1.0
Married	140	27.9
Separated	6	1.2
Single	342	68.1

Widowed/widower	9	1.8
Location		
Rural	105	20.9
Urban	397	79.1
Year of		
Presentation		
2019	155	30.9
2020	54	10.8
2021	113	22.5
2022	71	14.1
2023	109	21.7

Table 1: Shows that a total of five hundred and two (502) cases were seen over the period 2019 to 2023. The median age of the respondents was 28 years (range 60). The median age for females was 25, and the interquartile range is 11, while the median age for males was 31 years, and the interquartile range is 14. About 230 (45.8%) were those 20 -29 years old, followed by those 30 to 39 years old, 140 (27.9%). The majority, 342(68.1%) of them were singles, and more than half of them, 263 (52.4%) were males. The majority, 397 (79.1%), were from urban areas, and more cases were seen in 2019, 115 (30.9%), compared to the other years.

Table 2: Characteristics of cases seen at the Sexual and Reproductive Health clinic from 2019 to 2023.

Characteristics	Frequency	Percentage	
	n=502	(%)	
Type of Cases			
Follow-up cases	26	5.2	
New cases	467	93.0	
Not categorized	9	1.8	
Number of			
Sexual Partners			
in the Last 1 Year			
None	36	7.2	
One	207	41.2	
Two or more	209	41.6	
Unknown	50	10.0	
Number of			
Sexual Partners			
in the Last 3			
Months			
None	59	11.8	
One	289	74.4	
Two or more	129	25.7	
Unknown	25	5.0	
Condom Use			
Always	7	1.4	
Never	83	16.5	

Characteristics	Frequency	Percentage		
	n=502	(%)		
Sometimes	293	58.4		
Unknown	119	23.7		
Previous Histor of STI	у			
No	216	43.0		
Not Known	44	8.8		
Yes	242	48.2		
HIV Status				
Negative	315	62.7		
Not Known	105	20.9		
Positive	82	16.3		

Table 2 shows that the majority, 467 (93.0%) of the cases seen were new cases. About the same proportion, 207 (41.2%) had one or 209 (41.6%) multiple sexual partners in the last 1 year. The proportion of those with multiple sexual partners 3 months ago was 129 (25.7%), 293 (58.4%) used condoms sometimes, and 242 (48.2%) had a previous history of STI, while 82 (16.3%) cases were HIV positive.

Table 3: Pattern of STI cases seen at the Sexual and Reproductive Health clinic from 2019 to 2023.

Characteristics	Freq	Percent
	n=502	(%)
Pattern of STI Cases		
Multiple Syndromes	14	2.8
Genital Warts	132	26.3
Scabies	21	4.2
Fungal infections	41	8.2
Urethral Discharge Syndrome	41	8.2
Genital Ulcer Syndrome	35	7.0
Genital Herpes	35	7.0
Cervical Discharge Syndrome	19	3.8
Unknown	90	17.9
Others	74	14.7

Table 3 shows the pattern of STI cases seen at the clinic from 2019 to 2023. As shown, the most prevalent case seen is genital warts, 132 (26.3%).

Multiple syndromes is a combination of two or more cases for example, fungal infection and genital warts in the same patient. Unknown is for cases with no diagnosis written while others include pelvic inflammatory disease, galactorrhoea, uterine prolapse, cervical polyp, urinary tract infection and inguinal hernia.

There was a significant association between the pattern of STI cases and age ($\chi^2 = 110.26$; p < 0.001), sex ($\chi^2 =$



123.47; p < 0.001), marital status (χ^2 = 61.47; p < 0.005), and year of presentation (χ^2 = 93.85; p < 0.001). Genital warts are more common among age groups 10-19 years, 15 (33.3%), followed by age groups 20 to 29 years, 74 (32.2%). The highest proportion of genital warts was seen in the year 2023, 41 (37.6%), and the least was seen in 2019, 25(16.3%). A higher proportion of genital warts, 71 (29.1%) was seen among females compared to males, 61 (23.2%). Genital warts were more common among those separated 3(50.0%), followed by singles 108 (31.6%), then married 20 (14.5%).

Likewise, a higher proportion of those 10-19 years 6, 13.3%) had Scabies, followed by age groups 50 to 59 years 2, (7.7%). Scabies and Fungal infections were more common among singles, while genital ulcers and genital herpes were more common among those married. Fungal infections were common among those 70-79 years old (50.0%), and genital herpes was prevalent among those aged 50-59 years. A higher proportion of those 70-79 years 1 (50.0%) had fungal infections, followed by the age group 40 to 49 years 7 (12.7%). Genital herpes was more common among those 50 to 59 years 5, (19.2%), followed by age groups 30 to 39 years (14, 10.0%). Likewise, a higher proportion of fungal infection 39 (16.3%) was seen among females compared to males, 2 (0.8%). All those with multiple STI syndromes were females. Scabies, urethral discharge syndrome, genital ulcer syndrome, and herpes were more common in males than females. NGU = nongonococcal urethritis, CDS= cervical discharge syndrome, G U S = genital ulcer syndrome, MS = Multiple syndromes, others= (tinea, rape cases, PID, furunculosis, erectile dysfunction, urinary tract infection, and galactorrhoea)

Other factors that were significantly associated with the pattern of STI cases were HIV status ($\chi^2 = 38.32$; p \leq 0.004). and a previous history of STI ($\chi^2 = 28.53$; p \leq 0.054). Specifically, those who were HIV positive were shown to have higher proportions of multiple syndromes, genital warts, scabies, fungal infections, and genital ulcer syndrome compared to those who were HIV negative.

Those without a previous history of STI had a higher proportion of genital warts, 60(27.8%), compared to those with a previous history of STI, 61 (25.2%). Age at sexual debut, condom use, and location of residence were not shown to be associated factors.

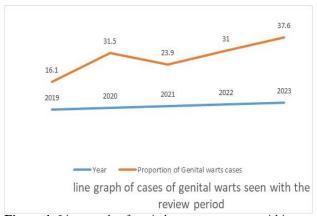


Figure 1: Line graph of genital warts cases seen within the period.

Figure 1 shows that the highest proportion of genital warts was seen in the year 2023, 41 (37.6%), and the least was seen in 2019, 25 (16.3%).



Table 4: Bivariate and multivariable analysis of sex differences in the pattern of STI cases seen

Variables	Sex (n=502)		cOR	p-value	aOR	p-value
	Female	Male	(95%CI)		(95%CI)	
	(n=239)	(n=263)				
	n(%)	n(%)				
Pattern of STI Cases						
Others R	34 (45.9)	40 (54.1)	0.90	0.74	1.1	0.74
Oulers K	34 (43.9)	40 (34.1)	(0.49-1.7)		(0.59-2.1)	
Multiple Syndrome	14 (100.0)	0 (0.0)	0.00	0.998		-
widiupic syndrome	14 (100.0)	0 (0.0)	(0.0-0.0)	0.770	_	
Genital Warts	71 (53.8)	61 (46.2)	0.66	0.127	1.5	0.127
Ocinical warts	71 (33.6)	01 (40.2)	(0.38-1.13)	0.127	(0.88-2.6)	
Scabies	1 (4.8) 20 (95.2) 15.3 0.009	0.009	0.07	0.009		
Scabics	1 (4.0)	20 (73.2)	(1.9-118.9)	0.007	(0.008-0.5)	
Fungal infections	39 (95.1)	2 (4.9)	0.4	0.001	25.5	0.001*
i ungai inicedons	37 (73.1)	2 (1.2)	(0.009 - 0.17)	0.001	(1.38-18.87)	
Urethral DS	4(9.8)	37(90.2)	7.1	0.001	0.14	0.001
0100000	.(>.0)	3 ((3 3.2)	(2.3-21.5)	3.301	(0.05 - 0.43)	
Genital Ulcer S	11 (31.4)	24(68.6)	1.7	0.225	0.56	0.225
	11 (31.1)	21(00.0)	(0.73-3.81)	0.223	(0.3-1.4)	
Genital Herpes	8 (22.9) 27 (77.1)	27 (77.1)	2.6	0.037	0.39	0.037*
•	` ,	, ,	(1.1-6.3)	0.007	(0.16 - 0.9)	
Cervical Discharge S	19 (100.0)	0 (0.0)	-	-	-	-
Unknown	39 (43.3)	51 (56.7)	-	-	-	-

^{*}Statistically significant (p<0.05); R=Reference value; cOR=crude Odds Ratio; aOR=adjusted Odds Ratio; DS= discharge syndrome; S= syndrome.

As shown in table 4, following a significant Chi-square test finding ($\chi^2 = 123.47$; p < 0.001), the multivariable analysis showed that there is a higher odd of scabies in males compared to females (cOR=15.3, 95% CI; 1.9-118.9, p=0.009), likewise, genital herpes (cOR=2.6, 95% CI; 1.1-6.3, p=0.037), . Whereas there is a higher odd of fungal infections in females compared to males (aOR=25.5, 95% CI; 1.38-18.87, p=0.001).

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DISCUSSION

We assessed the patterns and demographic factors associated with sexually transmitted infections (STI) in a tertiary health setting. The data from 502 cases observed over five years reveal a predominance of cases in younger adults, aged 20-29, followed by those aged 30-39. More than a quarter of the cases were cases of genital warts (the most prevalent case seen), with an increasing trend. Significant associations were found between STI patterns and age, sex, marital status, and year of presentation, HIV status, and a previous history of STI. Additionally, scabies and genital herpes were more common among males compared to females, while fungal infections where more common in females. There were no gender differences in the occurrence of genital warts.

Young adults 20-29, followed by those aged 30-39 were mostly affected. This is consistent with findings from other studies conducted in Ibadan, Nigeria. ¹⁵ However, their study reported more females, which is in contrast with the findings of this study; there were more males than females, and this is in tandem with another study in southwest Nigeria. ¹⁶ The findings also align with global trends indicating a higher prevalence of STI among individuals in their reproductive years. ^{7,8} This age group may be more sexually active, engage in high-risk behaviours, or have limited access to comprehensive sexual health education, highlighting a need for targeted preventive interventions. ⁶

Genital warts were most common among individuals aged 10-19 years and 20-29 years, suggesting that younger populations, particularly adolescents and young adults, are disproportionately affected by human papillomavirus (HPV) infections. This is consistent with findings from other studies conducted elsewhere, such as those by Devi et al.4 and Paudel et al.5, which also reported high rates of genital warts among STI clinic attendees. 4,5 This highlights the need for early sexual health education and vaccination efforts, particularly the introduction of the HPV vaccine to adolescents before sexual debut, as early exposure is a risk factor for HPV. The study reveals that men were more frequently diagnosed with STI, but some infections, like genital warts, were more common in women. This may be due to greater health-seeking behaviour among women or differences in biological susceptibility to HPV-related conditions. 1 Public health programs, especially HPV vaccination campaigns, should target both genders, but it's important to encourage males to seek care early, as male carriers can spread HPV without symptoms.

Scabies were also prevalent among males and those 10-19 age group, followed by those aged 50-59 years. This finding is in tandem with a study elsewhere that reported the highest prevalence among males and those 40 to 64 years. 17 It, however, contrasts with the study done in Ile-Ife by Ajana et al, which showed that sexually transmitted scabies was more prevalent among males in the 20-29 age group. 18 Scabies in younger age groups may reflect poor living conditions, overcrowding, or close contact in schools or communal environments. This also buttresses the need for public health programs to raise awareness of non-condom preventable STI among sexually active young adults. Health education regarding hygiene and preventive measures should be emphasised in schools, youth centres, and communities. Fungal infections were notably more common in females and older adults, particularly those aged 70-79 years and 40-49 years. This study agrees with a study done at Owerri, Imo State, where females were found to be more prone to sexually transmitted candidiasis when compared to males. However, this study also disagreed with the study done in Owerri, which suggested that fungal infections were more prevalent in the 26-30 (33.3%) year old age group. ¹⁹ This finding also contrasts with a previous institutional-based study that reported a higher prevalence among males²⁰. The higher prevalence in elderly individuals may be linked to age-related immune decline or comorbidities. Fungal infections in older adults could signal underlying health issues, such as diabetes or immune system compromise, and require thorough clinical evaluation. Fungal infections were also more frequent among females (16.3%) compared to males (0.8%), reflecting the fact that fungal infections is more common in women due to hormonal fluctuations and vaginal flora imbalances. This reinforces the need for sexual health education for sexually active adults, particularly around self-care and treatment for recurrent vaginal infections among women.

Genital herpes was most prevalent in individuals aged 50-59 years (19.2%), followed by those aged 30-39 years (10%). The presence of herpes in middle-aged adults has been shown in other studies. ^{21,22} This finding agrees with the study that was done by Chaabane et al, which also posited that the prevalence of genital herpes was higher in the age group of greater than 30 years (94.3%).²³ However, the findings of this study contrast



with the report of a study done at Gwagwalada, Abuja, which showed that the prevalence of genital herpes was higher among the 21-30 years age group. ²⁴ The presence of herpes in middle-aged adults suggests that herpes simplex virus (HSV) transmission remains active in sexually active adults. Middle-aged populations should not be overlooked in STI prevention efforts, and continuous education regarding HSV transmission and management is necessary. HIV-positive individuals had significantly higher proportions of multiple STI syndromes, genital warts, scabies, fungal infections, and genital ulcer syndrome compared to those who were HIV-negative. This co-occurrence of STIs in HIVpositive individuals can be explained by the immunocompromised state caused by HIV, which increases susceptibility to other infections. The observed association between STI and HIV status also reflects the known synergistic relationship between HIV and other STIs, as the presence of one can increase susceptibility to the other. 2

This finding emphasises the need for integrated STI and HIV care. Co-infection with STIs can accelerate HIV transmission, as ulcerative STIs such as genital ulcers can increase the likelihood of HIV transmission by creating entry points for the virus. Thus, comprehensive care and early treatment of STIs are crucial for HIV-positive individuals to reduce the risk of further transmission and complications.

The higher burden of STI in urban residents (79.1%) compared to rural residents may reflect the urban concentration of the clinic, but could also suggest behavioural and socioeconomic factors influencing STI transmission in densely populated settings ¹⁰. Addressing these findings with targeted community outreach, education, and accessible treatment options may improve STI outcomes.

Our findings were similar and contribute to the broader literature on STI epidemiology in sub-Saharan Africa. They support calls for enhanced sexual health education, improved accessibility of STI prevention resources, and more robust data collection systems to address health data poverty, a significant barrier to effective digital health and evidence-based practices. ^{9,11} Future research might focus on exploring specific behavioural determinants of STI transmission in Rivers State and assessing the impact of STI education interventions in reducing infection rates among high-risk groups.

Limitations, strength, and implication of the findings

The study is a retrospective review, data accuracy depends on existing records, with some missed or incomplete entries, with the diagnosis recorded as unknown. Also, the data were from a single facility/limited geographical area, the findings may not be generalizable to the wider population. Additionally, causal associations cannot be established due to the study design.

However, this study was based on 502 cases reviewed over five years, and provides quite a robust dataset for identifying trends, allowing for the observation of patterns and changes over time like the increasing trend in genital warts. The findings highlight the age groups most affected (20–29, 30–39 years), a valuable information for targeted public health interventions. The study provides sex-based variations providing clinically relevant insights and adds to the existing body of knowledge showing no sex difference in genital warts occurrence. Additionally, the findings provide evidence for STI prevention and control initiatives.

Conclusion

This study provides important insights into the demographic and behavioural patterns of STI cases from 2019 to 2023. Adolescents and young adults are disproportionately affected by genital warts, while older populations experience more fungal infections and herpes. There are notable sex differences in STI prevalence, with females being more likely to experience multiple STI syndromes, including genital warts and fungal infections, while males are more affected by scabies and urethral discharge and genital herpes. Marital status also plays a role, with singles and separated individuals showing higher rates of infection. The rising trend in genital warts cases over time highlights the need for intensified public health interventions and sustained STI prevention efforts across various population groups. HIV-positive individuals are disproportionately affected by multiple syndromes, genital warts, scabies, Fungal infections and genital ulcer syndromes, indicating a need for integrated care and targeted interventions. The increasing trend in genital warts cases, particularly in 2023, underscores the urgency of HPV vaccination efforts. Public health strategies should focus on early age and gender appropriate sexual health education, consistent use of preventive measures, and tailored interventions for high-risk groups like HIV-positive individuals and those with previous STI histories.

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Declarations

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Conflict of interest: Authors declare no conflict of interest

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