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High Burden of Symptomatic and Asymptomatic Sexually Transmitted Infections in a Routine Decentralised HIV Care Setting in Eswatini: A Cross-Sectional Study

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ABSTRACT

Objectives: Sexually transmitted infections are a global public health concern. We aimed to assess the burden of a diverse range of sexually transmitted infections in a high HIV burden setting in Eswatini and associated risk factors.

Methods: This cross-sectional study enrolled adults accessing routine outpatient care at six sites in Shiselweni, from July 2022 to April 2023. Laboratory investigations included antibody-based tests for HIV, *Treponema pallidum*, hepatitis B, hepatitis C, and herpes simplex 2 viruses. The molecular-based Xpert platform tested urine samples for *Chlamydia trachomatis*, *Neisseria gonorrhoea*, *Trichomonas vaginalis*, self-collected vaginal/anal swabs for Human papillomavirus, and plasma for HIV viremia. We calculated the proportion of laboratory-confirmed sexually transmitted infections among available test results and identified predictors of combined *Chlamydia trachomatis*/*Neisseria gonorrhoea*/*Trichomonas vaginalis* infection.

Results: Of 1396 study participants, 65.4% were women, the median age was 29 (IQR 23–36) years, and 19.6% were known HIV-positive. Overall, 68.6% had symptoms suggestive of *Chlamydia trachomatis*/*Neisseria gonorrhoea*/*Trichomonas vaginalis* infections. Laboratory-confirmed *Chlamydia trachomatis*/*Neisseria gonorrhoea*/*Trichomonas vaginalis* infection was found in 31.7% ($n = 443/1396$), of whom 20.8% were asymptomatic. Combined *Chlamydia trachomatis*/*Neisseria gonorrhoea*/*Trichomonas vaginalis* infections were common even among individuals with low risk of infection (e.g., no sexual intercourse: 20.7%) and were associated with young age, factory employment, and transactional sex. Prevalences for individual sexually transmitted infections were 16.9% ($n = 236/1394$) for *Chlamydia trachomatis*, 12.4% ($n = 173/1394$) for *Neisseria gonorrhoea*, 10.6% ($n = 148/1390$) for *Trichomonas vaginalis*, and 9.7% ($n = 135$) for *Treponema pallidum*. Viral infections were high for herpes simplex 2 viruses ($n = 792/1279$, 61.9%) and human papillomavirus ($n = 166/324$, 51.2%) and lower for hepatitis B virus ($n = 55/1396$, 3.9%) and hepatitis C virus ($n = 3/1396$, 0.2%). Of 1122 clients undergoing HIV testing, 4.1% ($n = 46/1122$) tested positive, with 21.7% ($n = 10/46$) being acute/early HIV infection.

Sustainable Development Goal: Good Health and Wellbeing

Conclusions: The substantial sexually transmitted infections burden highlights the urgent need to strengthen sexually transmitted infections service integration, expand access to affordable diagnostics, and target prevention in decentralised care. These findings support the development of context-adapted strategies to improve detection, treatment, and partner services in high-burden settings.

1 | Introduction

Sexually transmitted infections (STIs) pose a global public health challenge and cause over 1 million curable infections globally each day [1]. STIs often go untreated in resource-poor settings, causing morbidity and mortality [1, 2]. Untreated bacterial (*Chlamydia trachomatis* [CT], *Neisseria gonorrhoea* [NG]) or parasitic (*Trichomonas vaginalis* [TV]) STIs can cause sexual dysfunction, pelvic inflammatory disease, infertility, and adverse pregnancy outcomes [1, 3, 4]. The main viral STIs—HIV, Hepatitis B (HBV), Hepatitis C (HCV), Herpes simplex virus 2 (HSV-2), and Human papillomavirus (HPV)—can also lead to severe long-term health consequences if untreated, including hepatocellular carcinoma, cervical cancer, and severe immunodeficiency [1, 5, 6]. Therefore, early detection and treatment of both bacterial and viral STIs are essential.

STIs care is complex due to variable symptoms, asymptomatic cases, and drug-resistant strains [1, 7]. Socioeconomic vulnerabilities, poor healthcare access, and global public health threats increase infections and adverse outcomes in resource-poor settings [1, 8]. For instance, the COVID-19 pandemic weakened already under-resourced health systems [9, 10], potentially reducing access to STIs care [11]. In certain settings and populations, untreated bacterial and viral (e.g., HSV-2) infections are likely fuelling the HIV epidemic by elevating the risk of HIV transmission and acquisition [12–14]. In addition, while decentralised settings are crucial for bringing STI services closer to communities and are often nurse-led and supported by lay cadres, they frequently have limited access to advanced diagnostics beyond syndromic management compared to centralised, better-resourced settings. These factors combined likely contribute to weak STIs programmes, suboptimal care, and the unnoticed spread.

Understanding the STI burden across diverse contexts may help formulate targeted public health interventions. In high HIV-burden Eswatini, STIs were already prevalent before COVID-19. For instance, an estimated 46.2% of women of reproductive age were infected with HPV [15], while approximately 25.0% of young women seeking care at outpatient departments tested positive for CT, NG, or TV [16]. The impact of other infections such as HSV-2, HBV, and HCV remained largely undocumented. STI diagnosis was primarily syndromic, with rapid diagnostic tests available for HIV and for syphilis and hepatitis B in priority populations. Molecular testing was largely unavailable in the public sector due to cost. Therefore, we assessed the prevalence of STIs post COVID-19 in a routine decentralised care setting and identified risk factors linked to combined CT, NG, and TV infections for their potential application in targeted STIs care programming. We included a wide range of STIs, including HPV and HSV-2, to support an integrated approach, as these infections interact and partially overlap in risk factors, symptoms, and management strategies.

2 | Methods

2.1 | Setting

The predominantly rural Shisweleni region had an HIV prevalence of 26.5% in 2021 [17]. It comprised three secondary care facilities, approximately 23 primary care clinics, and a variety of community-based HIV testing sites. All sites provided integrated HIV and STIs care, offering routine screening for symptoms of STIs at the time of HIV diagnosis, and during antiretroviral therapy (ART) and HIV pre-exposure prophylaxis (PREP) care. Most clinic sites were equipped with rapid diagnostic tests (RDTs) that allowed routine testing for HIV, *Treponema pallidum* (TP), hepatitis B virus infection before PREP initiation, as well as urine-based leukocyte esterase and pregnancy testing.

2.2 | Study Design

This cross-sectional study (July 2022–April 2023) involved adults (≥18 years) accessing outpatient consultations, HIV testing, and ART care in Shiselweni. Individuals who had received STI treatment within the past month were excluded. Health structures comprised one secondary and three primary care clinics and two community-based care points. These care sites differed in size, setting, and target population (Table 1). The study was implemented by Médecins Sans Frontières (MSF) in collaboration with the Ministry of Health.

2.3 | Study Procedures

Clients seeking routine HTS, ART initiation and follow-up care, and those diagnosed with STIs through the syndromic approach in general outpatient consultations were invited to participate in the study. Upon obtaining written consent, participants completed a self-questionnaire that was available electronically or on paper. The questionnaire assessed sociodemographic and behavioural factors, as well as self-reported urogenital symptoms suggestive of STIs. Then, HTS counsellors who also acted as phlebotomists conducted routine HIV testing and obtained whole venous blood. They also prepared patient self-collected urine samples and self-collected vaginal and rectal (men only) swabs for shipment to Nhlangano laboratory.

At the laboratory, technicians prepared samples for shipment to the National Institute for Communicable Diseases (NICD) in

TABLE 1 | Details on the characteristics of the study sites.

Study site	Site characteristics	Care level	Highest level of staff	Client volume	Target populations						
					General population	Young people	Factory workers	Men	MSM	Sex workers	Truck drivers
Nhlangano facility	Urban	Secondary care	Doctors & nurses	High	x						
Factory clinic	Semi-urban	Primary care	Nurses	Medium			x				
Primary care clinic 1	Rural	Primary care	Nurses	Medium	x						
Primary care clinic 2	Rural	Primary care	Nurses	Medium	x						
Nhlangano fixe site	Urban	Community care	Nurses	Low	x[a]	x		x	x		
Lavumisa fixed site	Semi-urban	Community care	Nurses	Low	x					x	x

Abbreviations: ART, antiretroviral therapy; HTS, HIV testing services; MSM, men who have sex with men; STIs, sexually transmitted infections.

[a]This site also provided access to the general population although the main target was other populations. Community site 1 was solely staffed by MSF, community site 2 by MSF and MOH staff, and all other sites mainly by MOH staff. All sites provided HTS, HIV prevention (PEP, PREP, condoms), ART initiation, ART follow-up care (but not Fixed site [taxi rank]), reproductive care, and STIs screening and syndromic STIs management.

South Africa for HSV-2 testing (HerpeSelect 2 ELISA IgG Assay). On-site, urine samples were tested for CT, NG, and TV using the molecular-based Xpert platform. In addition, plasma samples were used to test for HIV viral load for the detection of acute and early HIV (AEHIV) infection, and vaginal/anal (men) swabs for the detection of HPV by Xpert. Routine immunoglobulin-based lateral flow RDTs were used for testing for established HIV, HBV, HCV, and TP. In case of positive TP results, samples were forwarded to the national reference laboratory for rapid plasma reagin (RPR) testing. Routine internal and external quality control measures were conducted according to standard protocols of the Eswatini National Reference Laboratory and manufacturers' instructions.

At the clinic, tests conducted by phlebotomists included routine HIV testing (serial RDT testing algorithm using Determine HIV-1/2 and Uni-Gold HIV), pregnancy testing (HCG urine strip), and urine leucocyte esterase strip tests. Nurses, following the syndromic approach, assessed the presence of STIs, and treatment was provided according to national guidelines [18]. Asymptomatic clients testing positive were recalled to the clinic for further assessment and treatment adjustments in accordance with the identified pathogen. Clients diagnosed with STIs were provided with partner notification slips and offered partner-assisted notification services.

2.4 | Main Definitions

Symptomatic presentation at study entry was defined as clients presenting with any of the following self-reported symptoms: genital itchiness or discharge, pain when urinating or during sex, abdominal pain in women, and scrotal swelling in men.

Combined CT/NG/TV infection was defined as the presence of one or more of the pathogens CT, NG, or TV as detected by Xpert. Asymptomatic infections with CT/NG/TV were defined as clients presenting with combined CT/NG/TV infection in the absence of self-reported symptoms. Male urethritis syndrome (MUS) and vaginal discharge syndrome (VDS) were defined as screening diagnoses made by clinicians using the syndromic approach.

AEHIV infection was defined as a negative or discordant HIV test result according to the serial RDT algorithm with a HIV viral load of ≥ 20 copies/mL [19], regardless of symptoms such as sore throat, fever, or skin rash. Established HIV infection was defined as reactivity to both serial HIV RDTs and irrespective of HIV viral load test results.

2.5 | Statistics

All analyses were conducted using Stata 18.0. Categorical variables were described using frequency statistics and proportions. Continuous variables were presented as medians and interquartile ranges (IQRs).

To measure the burden of STIs for the overall study population and for different baseline factors, we calculated the proportion

of clients who had a positive laboratory test result for any STIs out of the available test results.

Associations of baseline factors with CT/NG/TV infection were determined through univariate and multivariable logistic regression. Variables with a p-value ≤ 0.15 from the univariate analysis were included in backward stepwise logistic regression until only those factors with a p-value ≤ 0.05 remained associated with the outcome.

2.6 | Ethics

This study was approved by the Eswatini Health and Human Research Review Board (EHHRRB096/2021) and the MSF Ethics Review Board (ID: 2154).

3 | Results

Figure 1 presents the study flow. Among the 1483 clients eligible for the study, 87 (5.9%) were excluded due to missing baseline information. Consequently, 1396 (94.1%) participants were included in the analysis.

3.1 | Client Characteristics at Enrolment

Among all study participants ($n = 1396$) (Table 2, Part-1), 274 (19.6%) were aware of their HIV-positive status, with the remaining 1122 (80.4%) individuals undergoing HIV testing. The majority were women ($n = 913$, 65.4%) of whom 27.8% ($n = 254/913$) were either pregnant or breastfeeding. The median age was 29 (IQR 23–36) years. Individuals accessed various care sites including one factory clinic ($n = 195$, 14.0%). Most individuals reported some educational background, and nearly half ($n = 623$, 44.9%) were unemployed. Most were in a relationship ($n = 1262$, 92.1%), and almost a third acknowledged having two or more sexual partners ($n = 431/1394$, 30.9%), with 13.1% ($n = 165/1260$) reporting an age difference of ≥ 10 years with their primary partner. Key behavioural risk factors included alcohol use during intercourse (20.7%), condomless intercourse (74.7%), and exposure to body fluids (52.6%) within the last 6 months. Reported transactional sex, injectable drug use, and anal sex were all below 6%. Around a quarter reported an STIs in the past year, and over half perceived themselves at risk of contracting STIs.

3.1.1 | Self-Reported Symptoms and Syndromic Diagnosis

Symptoms suggestive of CT/NG/TV infections were prevalent in 68.6% ($n = 958/1396$) of individuals (Table 2 and Figure 2). The most common symptom was abdominal pain in women (52.7%), followed by about one third of individuals reporting genital itchiness (35.9%) and genital discharge (34.2%). About a quarter reported pain when urinating (26.1%) and during intercourse (23.6%). Self-reported scrotal swelling (4.6%) in men was less common. In addition, 28.01% ($n = 391$) individuals screened positive for VDS/MUS, with 250 (27.4%) women presenting with VDS and 141 (29.2%) men with MUS, respectively.

3.2 | Overall STI Prevalence

Table 3 presents the STIs testing outcomes.

3.2.1 | CT, NG, TV

The proportion of individual infections was 16.9% ($n = 236/1394$) for CT, 12.4% ($n = 173/1394$) for NG, and 10.6% ($n = 148/1390$) for TV. The proportion of combined CT/NG/TV infection was 31.7% ($n = 443/1396$). Out of these participants, 90 (20.3%) and 12 (2.7%) had coinfections with two and three of these pathogens.

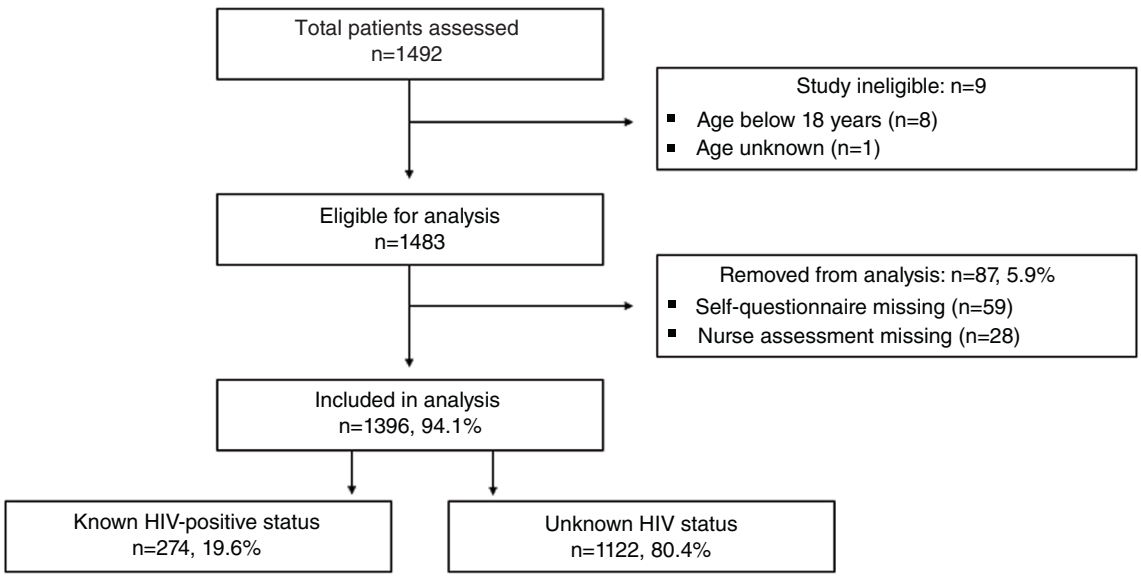

FIGURE 1 | Study flow chart. Enrolment of individuals with already known HIV status intentionally ceased at around 20% of the total study cohort, following the study protocol.

TABLE 2 | Baseline characteristics of patients undergoing molecular-based testing for CT/NG/TV pathogens (Part-1), their testing outcomes by baseline characteristics (Part-2), and prevalence estimates of CT/NG/TV among tested population (Part-3).

	Part-1: Tested for CT/NG/TV		Part-2: CT/NG/TV infection status					Part-3: Prevalence of CT/NG/TV
			Negative		Positive			Detected
	n	% (col)	*n*	% (col)	*n*	% (col)	*p*-value	% (row)[c]
Facility								
Nhlangano	445	(31.9)	300	(31.5)	145	(32.7)	< 0.001	(32.6)
Factory clinic	195	(14.0)	105	(11.0)	90	(20.3)		(46.2)
Primary care clinic 1	172	(12.3)	124	(13.0)	48	(10.8)		(27.9)
Primary care clinic 2	134	(9.6)	101	(10.6)	33	(7.4)		(24.6)
Nhlangano fixed site	214	(15.3)	155	(16.3)	59	(13.3)		(27.6)
Lavumisa fixed site	236	(16.9)	168	(17.6)	68	(15.3)		(28.8)
Entry point								
OPD	319	(22.9)	195	(20.5)	124	(28.0)	0.003	(38.9)
ART care	179	(12.8)	134	(14.1)	45	(10.2)		(25.1)
HTS	898	(64.3)	624	(65.5)	274	(61.9)		(30.5)
HIV status prior HTS								
Known HIV-positive	274	(19.6)	196	(20.6)	78	(17.6)	0.195	(28.5)
Unknown/negative HIV status	1122	(80.4)	757	(79.4)	365	(82.4)		(32.5)
Age, years								
18–29	754	(54.0)	466	(48.9)	288	(65.0)	< 0.001	(38.2)
30–39	409	(29.3)	298	(31.3)	111	(25.1)		(27.1)
40–49	176	(12.6)	138	(14.5)	38	(8.6)		(21.6)
≤ 50	57	(4.1)	51	(5.4)	6	(1.4)		(10.5)
Sex								
Female	913	(65.4)	627	(65.8)	286	(64.6)	0.652	(31.3)
Male	483	(34.6)	326	(34.2)	157	(35.4)		(32.5)
Pregnancy status[a]								
Negative	1182	(84.7)	809	(84.9)	373	(84.2)	0.323	(31.6)
Uncertain	54	(3.9)	32	(3.4)	22	(5.0)		(40.7)
Yes	160	(11.5)	112	(11.8)	48	(10.8)		(30.0)
Breastfeeding[a]								
No	1302	(93.3)	883	(92.7)	419	(94.6)	0.181	(32.2)
Yes	94	(6.7)	70	(7.3)	24	(5.4)		(25.5)
Education level completed								
None completed	33	(2.4)	24	(2.5)	9	(2.1)	< 0.001	(27.3)
Primary	164	(11.8)	108	(11.4)	56	(12.8)		(34.1)
Secondary	341	(24.6)	222	(23.4)	119	(27.1)		(34.9)

(Continues)

TABLE 2 | (Continued)

	Part-1: Tested for CT/NG/TV		Part-2: CT/NG/TV infection status					Part-3: Prevalence of CT/NG/TV
			Negative		Positive			Detected
	n	% (col)	*n*	% (col)	*n*	% (col)	*p*-value	% (row)[c]
High school	634	(45.7)	416	(43.8)	218	(49.7)		(34.4)
Tertiary	216	(15.6)	179	(18.9)	37	(8.4)		(17.1)
Employment status								
Employed	537	(38.7)	366	(38.6)	171	(38.8)	0.074	(31.8)
Self-employed	144	(10.4)	111	(11.7)	33	(7.5)		(22.9)
Casual worker	85	(6.1)	53	(5.6)	32	(7.3)		(37.6)
Unemployed	623	(44.9)	418	(44.1)	205	(46.5)		(32.9)
Behaviour factors								
In a relationship								
No	108	(7.9)	86	(9.2)	22	(5.1)	0.009	(20.4)
Yes	1262	(92.1)	852	(90.8)	410	(94.9)		(32.5)
Wish for a child								
No	950	(68.4)	658	(69.3)	292	(66.5)	0.295	(30.7)
Yes	366	(26.4)	239	(25.2)	127	(28.9)		(34.7)
Uncertain	72	(5.2)	52	(5.5)	20	(4.6)		(27.8)
Last sexual intercourse (past 6 months)								
No intercourse	58	(4.2)	46	(4.8)	12	(2.7)	0.013	(20.7)
< 1 month	1061	(76.3)	705	(74.1)	356	(81.1)		(33.6)
≥ 1 month	271	(19.5)	200	(21.0)	71	(16.2)		(26.2)
Number of sexual partners (past 6 months)								
None	58	(4.2)	53	(5.6)	5	(1.1)	< 0.001	(8.6)
1	905	(64.9)	644	(67.7)	261	(58.9)		(28.8)
2	321	(23.0)	190	(20.0)	131	(29.6)		(40.8)
≥ 3	110	(7.9)	64	(6.7)	46	(10.4)		(41.8)
Age difference with main partner, years								
< 5 years	669	(53.1)	461	(53.2)	208	(52.9)	0.994	(31.1)
5–9 years	426	(33.8)	293	(33.8)	133	(33.8)		(31.2)
≥ 10 years	165	(13.1)	113	(13.0)	52	(13.2)		(31.5)
Alcohol use before sex (past 6 months)								
No	1036	(79.3)	729	(82.5)	307	(72.7)	< 0.001	(29.6)
Yes	270	(20.7)	155	(17.5)	115	(27.3)		(42.6)

(Continues)

TABLE 2 | (Continued)

	Part-1: Tested for CT/NG/TV		Part-2: CT/NG/TV infection status					Part-3: Prevalence of CT/NG/TV
			Negative		Positive			Detected
	n	% (col)	*n*	% (col)	*n*	% (col)	*p*-value	% (row)[c]
Injectable drug use since last HTS								
No	1294	(98.4)	880	(98.4)	414	(98.3)	0.896	(32.0)
Yes	21	(1.6)	14	(1.6)	7	(1.7)		(33.3)
Provided goods for sex								
No	1235	(95.4)	836	(96.1)	399	(93.9)	0.076	(32.3)
Yes	60	(4.6)	34	(3.9)	26	(6.1)		(43.3)
Received goods for sex							0.020	
No	1224	(94.4)	832	(95.4)	392	(92.2)		(32.0)
Yes	73	(5.6)	40	(4.6)	33	(7.8)		(45.2)
Condomless sex (past 6 months)								
No	335	(25.3)	232	(26.1)	103	(23.8)	0.371	(30.7)
Yes	988	(74.7)	658	(73.9)	330	(76.2)		(33.4)
Anal sex (past 6 months)								
No	1255	(95.7)	843	(95.6)	412	(95.8)	0.844	(32.8)
Yes	57	(4.3)	39	(4.4)	18	(4.2)		(31.6)
Exposed to body fluids (past 6 months)								
No	639	(47.4)	428	(46.4)	211	(49.5)	0.280	(33.0)
Yes	710	(52.6)	495	(53.6)	215	(50.5)		(30.3)
Feeling at risk of STIs (past 6 months)								
No	497	(36.7)	363	(39.5)	134	(30.8)	0.007	(27.0)
Yes	737	(54.4)	481	(52.3)	256	(58.9)		(34.7)
Uncertain	120	(8.9)	75	(8.2)	45	(10.3)		(37.5)
STI diagnosed (past 6 months)								
No	1019	(73.4)	687	(72.5)	332	(75.5)	0.241	(32.6)
Yes	369	(26.6)	261	(27.5)	108	(24.5)		(29.3)
Sexual partner had STIs (past 6 months)								
No	800	(57.3)	557	(58.4)	243	(55.0)	0.475	(30.4)
Yes	219	(15.7)	146	(15.3)	73	(16.5)		(33.3)
Unknown	376	(27.0)	250	(26.2)	126	(28.5)		(33.5)

(Continues)

TABLE 2 | (Continued)

	Part-1: Tested for CT/NG/TV		Part-2: CT/NG/TV infection status					Part-3: Prevalence of CT/NG/TV
			Negative		Positive			Detected
	n	% (col)	*n*	% (col)	*n*	% (col)	*p*-value	% (row)[c]
Considering partner notification if STI positive								
No	152	(11.2)	98	(10.6)	54	(12.5)	0.582	(35.5)
Yes	1152	(85.1)	789	(85.6)	363	(84.0)		(31.5)
Uncertain	50	(3.7)	35	(3.8)	15	(3.5)		(30.0)
Symptoms								
Genital itchiness								
No	895	(64.1)	618	(64.8)	277	(62.5)	0.400	(30.9)
Yes	501	(35.9)	335	(35.2)	166	(37.5)		(33.1)
Genital sores								
No	1203	(86.2)	817	(85.7)	386	(87.1)	0.479	(32.1)
Yes	193	(13.8)	136	(14.3)	57	(12.9)		(29.5)
Pain when urinating								
No	1032	(73.9)	769	(80.7)	263	(59.4)	< 0.001	(25.5)
Yes	364	(26.1)	184	(19.3)	180	(40.6)		(49.5)
Pain during intercourse								
No	1067	(76.4)	736	(77.2)	331	(74.7)	0.303	(31.0)
Yes	329	(23.6)	217	(22.8)	112	(25.3)		(34.0)
Genital discharge								
No	919	(65.8)	696	(73.0)	223	(50.3)	< 0.001	(24.3)
Yes	477	(34.2)	257	(27.0)	220	(49.7)		(46.1)
Abdominal pain								
No	831	(59.5)	566	(59.4)	265	(59.8)	0.879	(31.9)
Yes	565	(40.5)	387	(40.6)	178	(40.2)		(31.5)
Symptomatic presentation[b]								
No	438	(31.4)	346	(36.3)	92	(20.8)	0.000	(21.0)
Yes	958	(68.6)	607	(63.7)	351	(79.2)		(36.6)
VDS/MUS								
No	1005	(72.0)	758	(79.5)	247	(55.8)	0.000	(24.6)
Yes	391	(28.0)	195	(20.5)	196	(44.2)		(50.1)

Abbreviations: ART, antiretroviral therapy; CT, *Chlamydia trachomatis*; HTS, HIV testing services; MUS, male urethritis syndrome; *n*, number; NG, *Neisseria gonorrhoeae*; OPD, general outpatient department; STIs, sexually transmitted infections; TV, *Trichomonas vaginalis*; VDS, vaginal discharge syndrome.
[a]For analysis, males were coded as not being pregnant or breastfeeding. Restricted to females, 17.5% ($n = 160/913$) were pregnant, while 10.3% ($n = 94/913$) were breastfeeding.
[b]Symptomatic presentation at study entry was defined as clients presenting with any of the following self-reported symptoms, comprising genital itchiness or discharge, pain when urinating or during sex, abdominal pain in women, and scrotal swelling in men.
[c]The denominator is the number of clients tested for CT/NG/TV pathogens.

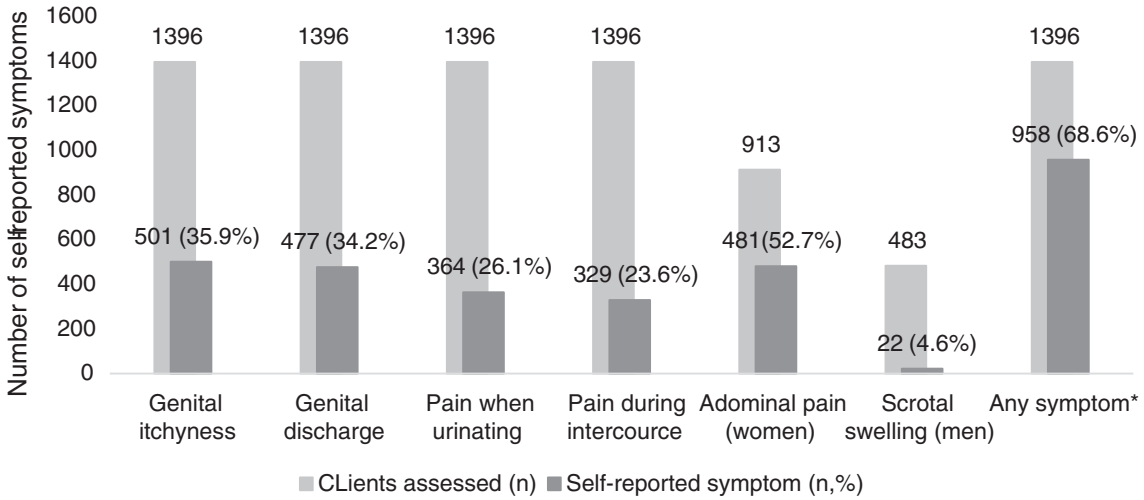

FIGURE 2 | The total number assessed and the proportion of individuals with self-reported symptoms suggestive of CT/NG/TV infection. *These are individuals who reported at least one or a combination of symptoms suggestive for CT/NG/TV infection.

TABLE 3 | The number of tests performed per STI, and the proportion of individuals with positive test results.

	Total test results	Positive test results	
Pathogens tested	**Number**	**Number**	**Percentage (95% confidence intervals)**
CT/NG/TV	1396	443	31.7 (29.3–34.2)
CT	1394	236	16.9 (15.0–19.0)
NG	1394	173	12.4 (10.8–14.2)
TV	1390	148	10.6 (9.1–12.4)
TP	1396	135	9.7 (8.2–11.3)
HBV	1396	55	3.9 (3.0–5.1)
HCV	1396	3	0.2 (0.1–0.7)
HPV	324	166	51.2 (45.8–56.7)
HSV-2	1275	792	62.1 (59.4–64.7)
AEHIV	1112	10	0.9 (0.4–1.6)
Established HIV	1112	36	3.2 (2.3–4.5)
Total HIV	1112	46	4.1 (3.0–5.5)

Abbreviations: AEHIV, acute and early HIV infection; CT, *Chlamydia trachomatis*; CT/NG/TV, combined *Chlamydia trachomatis*, *Neisseria gonorrhoeae* and *Trichomonas vaginalis* infection; HBV, hepatitis B virus; HCV, hepatitis C virus; HPV, human papillomavirus; HSV-2, herpes simplex virus type 2; NG, *Neisseria gonorrhoeae*; TP, *Treponema pallidum*; TV, *Trichomonas vaginalis*.

Figure 3 shows the 15 factors with the highest prevalence estimates of combined CT/NG/TV infections. These infections were particularly prevalent among clients with some self-reported symptoms, those with VDS or MUS (50.1%), clients attending the factory clinic (46.2%), and clients engaging in transactional sex (buying sex: 43.3%; selling sex: 45.2%).

Individuals presenting with low-risk factors for CT/NG/TV infection also had important prevalence of these infections (Table 2, Part-3). They included not being in a relationship (20.4%), reporting no intercourse within the last 6 months (20.7%), having no sexual partner (8.6%), and not perceiving themselves at risk of STIs (27.0%) infection in the preceding 6 months.

Additionally, clients lacking clear clinical presentations suggestive of infection displayed significant proportions of CT/NG/TV infection, including the absence of VDS/MUS (24.6%), asymptomatic presentation (21.0%) or lack of these self-reported symptoms with prevalences ranging from 24.3% to 32.1% (Table 2, Part-3).

3.2.2 | TP

Among all study participants, 9.7% ($n = 135$) showed a positive result for TP using the standard RDT. Among them, 109 (80.7%) had RPR testing results, with 107 (98.2%) displaying reactivity, of whom 54.2% exhibited low-level (1:1, 1:2) and 23.4% medium-level (1:8, 1:16) reactive titres.

3.2.3 | HSV-2

Out of 1279 participants with available HSV-2 test results, the majority tested positive ($n = 792$, 61.9%), while 4 (0.3%) individuals received equivocal test results necessitating further testing.

3.2.4 | HIV

Out of 1122 individuals undergoing HIV testing, 46 (4.1%) tested positive. Among these cases, 78.3% ($n = 36/46$) had established HIV infection, and 21.7% ($n = 10/46$) presented with AEHIV.

3.2.5 | HBV & HCV

Overall, 55/1396 (3.9%) tested positive for HBV infection. Of these, 18 (32.7%) received ART due to HIV coinfection, with a

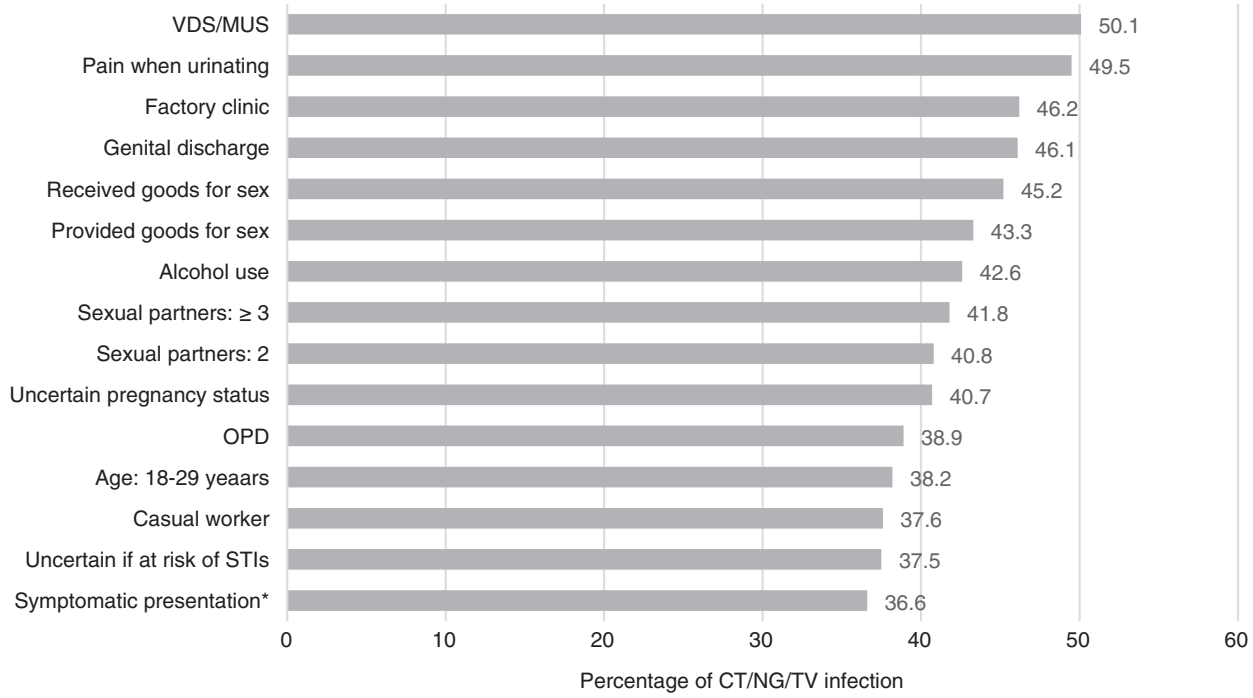

FIGURE 3 | Fifteen factors ordered by highest prevalence estimates of combined CT/NG/TV infections. MUS, male urethral discharge syndrome; OPD, outpatient department; STIs, sexually transmitted infections; VDS, vaginal discharge syndrome. *Symptomatic presentation at study entry was defined as clients presenting with any of the following self-reported symptoms, comprising genital itchiness or discharge, pain when urinating or during sex, abdominal pain in women, and scrotal swelling in men.

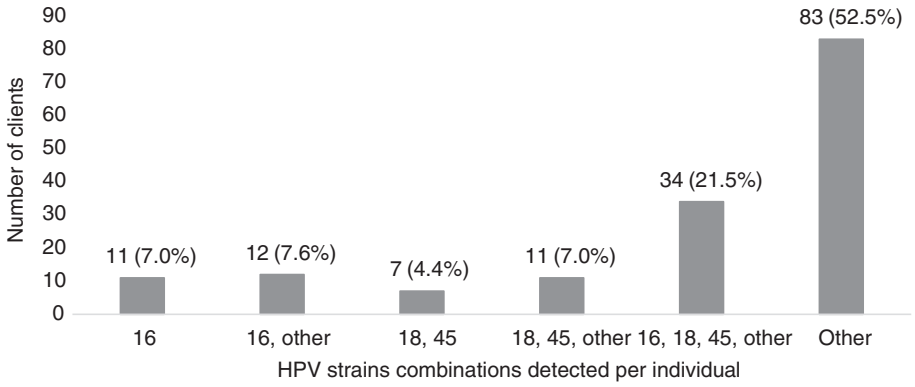

FIGURE 4 | Distribution of HPV strain combinations detected among men and women. Of 166 men and women testing positive for HPV infection, 158 (95.2%) had a strain result available. The category other strains comprise strain number 31, 33, 35, 39, 51, 52, 56, 58, 59, and 68. The categories of HPV strains are mutually exclusive.

median HBV viral load of 0 (IQR 0–23) IU/mL. The remaining 37 (67.3%) individuals were ART naïve and had a higher median viral load (335 IU/mL, IQR 16–2470) ($p < 0.001$). Only 3/1396 (0.2%) individuals presented with HCV infection, all of whom had an undetectable viral load.

3.2.6 | HPV

Of 324 clients undergoing testing for HPV, 166 (51.2%) had a positive test result. Positivity was lower in men ($n = 10/37$, 27.0%) vs. in women ($n = 156/284$, 54.9%). Among participants with available HPV strain results ($n = 158$) (Figure 4), nearly half ($n = 75/158$, 47.5%) were found to have either strain 16, 18, or 45, or a combination thereof, with or without the presence of other strains.

3.3 | Prevalence of Main Coinfections

3.3.1 | HIV and Other STI Coinfections

Figure 5 shows the prevalence of STI coinfections by HIV status after HIV testing. Significant differences were observed for NG, TV, TP, and HSV-2, with a tendency for higher prevalence among new HIV-positive participants for NG (15.2%; $p = 0.035$), TV (21.7%; $p = 0.001$), and TP (21.7%; $p < 0.001$). For HSV-2, prevalence was high among

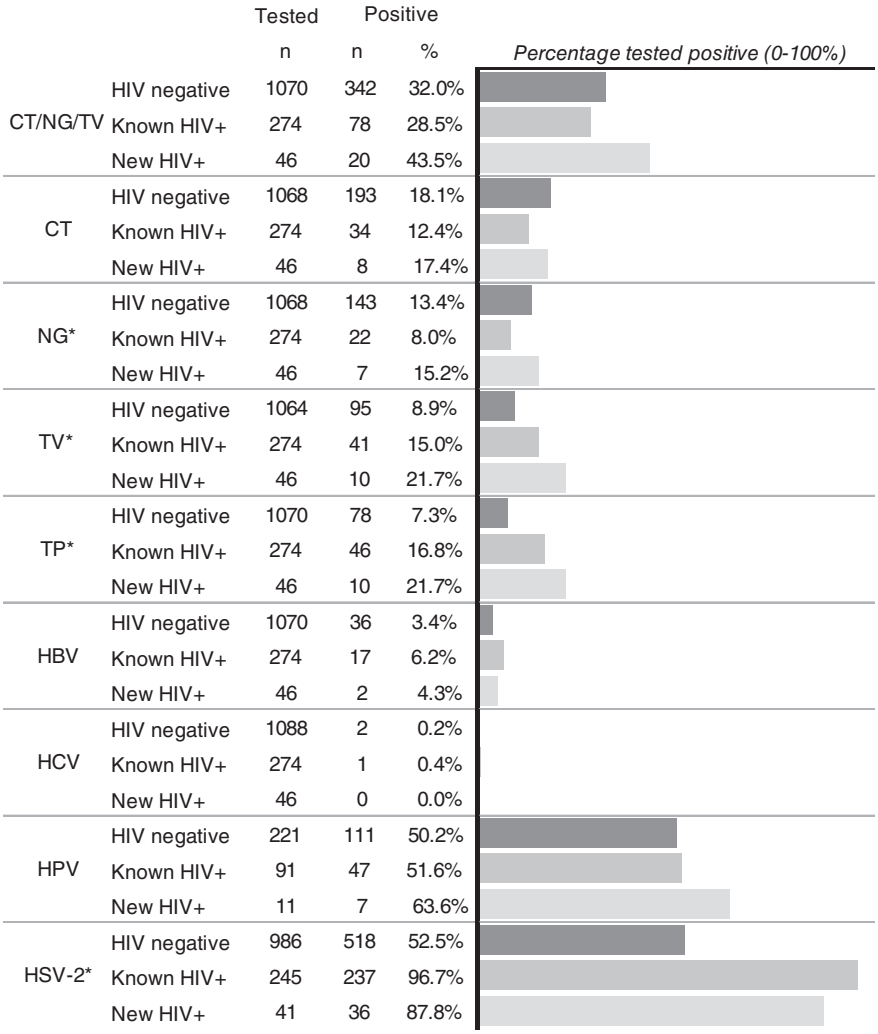

FIGURE 5 | Prevalence of STI coinfections by HIV status after HIV testing among study participants. %, percentage; CT, *Chlamydia trachomatis*; CT/NG/TV, combined *Chlamydia trachomatis*, *Neisseria gonorrhoeae* and *Trichomonas vaginalis* infection; HBV, hepatitis B virus; HCV, hepatitis C virus; HIV+, HIV-positive; HPV, human papillomavirus; HSV-2, herpes simplex virus type 2; MUS, male urethral discharge syndrome; *n*, number; NG, *Neisseria gonorrhoeae*; OPD, outpatient department; STIs, sexually transmitted infections; TP, *Treponema pallidum*; TV, *Trichomonas vaginalis*; VDS, vaginal discharge syndrome. Known HIV+ refers to participants who were aware of their HIV-positive status prior to study enrolment. New HIV+ and HIV-negative refer to participants whose HIV status was newly established through testing in the study (new HIV+ includes established and acute/early HIV infection). Six cases were excluded from this analysis because their HIV status remained unknown. HSV-2 prevalence includes only clients with clearly reactive positive test results while equivocal test results were excluded from the analysis (1 among known HIV-positive cases and 3 among HIV-negative cases). *Fisher's exact test for differences in coinfection across HIV status was significant for NG ($p = 0.035$), TV ($p = 0.001$), TP ($p < 0.001$), and HSV-2 ($p < 0.001$).

HIV-positive participants overall (new HIV-positive: 87.8%; known HIV-positive: 96.7%) compared to HIV-negative participants (52.5%; $p < 0.001$).

3.3.2 | CT/NG/TV and Other STI Coinfections

Among clients diagnosed with combined CT/NG/TV infection and with available test results for other STIs, the rates of coinfection were as follows: 16/443 (3.6%) had HBV, 1/443 (0.2%) had HCV, 261/405 (64.4%) had HSV-2, 60/113 (53.1%) had HPV, 20/362 (5.5%) had HIV infection comprising 15 chronic and 5 AEHIV cases, and 60/443 (13.5%) had TP, respectively.

3.4 | Associations With Combined CT/NG/TV Infection

Table 2 (Part-2) presents the distribution of client characteristics according to CT/NG/TV infection status. In crude analysis, factors such as facility type, clinic entry point, age, social factors (education, employment), various behavioural determinants (e.g., engagement in transactional sex), self-reported symptoms (e.g., pain during urination and genital discharge), and positive screening results for VDS/MUS appeared to be associated with CT/NG/TV infection.

In multivariable analysis (Table 4), the odds of CT/NG/TV infection tended to be higher for the factory clinic (aOR 1.45,

TABLE 4 | Univariate and multivariable analysis for the association between baseline factors and combined CT/NG/TV infection.

	cOR		aOR ($n = 1297$)	
Facility				
Nhlangano	1		1	
Factory clinic	1.77	(1.26–2.50)	1.45	(0.99–2.13)
Primary care clinic 1	0.80	(0.54–1.18)	1.07	(0.70–1.65)
Primary care clinic 2	0.68	(0.44–1.05)	0.65	(0.40–1.05)
Nhlangano fixed site	0.79	(0.55–1.13)	0.62	(0.42–0.93)
Lavumisa fixed site	0.84	(0.59–1.18)	0.78	(0.53–1.15)
Entry point				
OPD	1			
ART care	0.53	(0.35–0.79)		
HTS	0.69	(0.53–0.90)		
HIV status prior HTS				
Known HIV-positive	1			
Unknown/negative HIV status	1.21	(0.91–1.62)		
Age, years				
18–29	1		1	
30–39	0.60	(0.46–0.78)	0.61	(0.45–0.81)
40–49	0.45	(0.30–0.66)	0.56	(0.36–0.86)
≤ 50	0.19	(0.08–0.45)	0.32	(0.13–0.79)
Sex				
Female	1			
Male	1.06	(0.83–1.34)		
Pregnancy status				
Negative	1			
Uncertain	1.49	(0.85–2.60)		
Yes	0.93	(0.65–1.33)		
Breastfeeding				
No	1			
Yes	0.72	(0.45–1.17)		
Education level completed				
None completed	1			
Primary	1.38	(0.60–3.18)		
Secondary	1.43	(0.64–3.17)		
High school	1.40	(0.64–3.06)		
Tertiary	0.55	(0.24–1.28)		
Employment status				
Employed	1			
Self-employed	0.64	(0.41–0.98)		

(Continues)

TABLE 4 | (Continued)

	cOR		aOR ($n = 1297$)	
Casual worker	1.29	(0.80–2.08)		
Unemployed	1.05	(0.82–1.34)		
In a relationship				
No	1			
Yes	1.88	(1.16–3.05)		
Wish for a child				
No	1			
Yes	1.20	(0.93–1.55)		
Uncertain	0.87	(0.51–1.48)		
Last sexual intercourse (past 6 months)				
No intercourse	1			
< 1 month	1.94	(1.01–3.70)		
≥ 1 month	1.36	(0.68–2.71)		
Number of sexual partners (past 6 months)				
0	1			
1	4.30	(1.70–10.87)	0.62	(0.40–0.96)
2	7.31	(2.84–18.78)	0.86	(0.54–1.38)
≥ 3	7.62	(2.82–20.55)	[b]	
Age difference with main partner, years				
< 5 years	1			
5–9 years	1.01	(0.77–1.31)		
≥ 10 years	1.02	(0.71–1.47)		
Alcohol use before sex (past 6 months)				
No	1			
Yes	1.76	(1.34–2.32)		
Injectable drug use since last HTS				
No	1			
Yes	1.06	(0.43–2.65)		
Provided goods for sex				
No	1			
Yes	1.60	(0.95–2.71)		
Received goods for sex				
No	1			
Yes	1.75	(1.09–2.82)	1.89	(1.12–3.18)
Condomless sex (past 6 months)				
No	1			
Yes	1.13	(0.86–1.48)		

(Continues)

TABLE 4 | (Continued)

	cOR		aOR ($n = 1297$)	
Anal sex (past 6 months)				
No	1			
Yes	0.94	(0.53–1.67)		
Exposed to body fluids (past 6 months)				
No	1			
Yes	0.88	(0.70–1.11)		
Feeling at risk of STIs (past 6 months)				
No	1			
Yes	1.44	(1.12–1.85)		
Uncertain	1.63	(1.07–2.47)		
STI diagnosed (past 6 months)				
No	1			
Yes	0.86	(0.66–1.11)		
Sexual partner had STIs (past 6 months)				
No	1			
Yes	1.15	(0.83–1.58)		
Unknown	1.16	(0.89–1.50)		
Considering partner notification if STI positive				
No	1			
Yes	0.83	(0.59–1.19)		
Uncertain	0.78	(0.39–1.55)		
Genital itchiness				
No	1			
Yes	1.11	(0.87–1.40)		
Genital sores				
No	1			
Yes	0.89	(0.64–1.24)		
Pain when urinating				
No	1		1	
Yes	2.86	(2.23–3.67)	1.86	(1.39–2.49)
Pain during intercourse				
No	1			
Yes	1.15	(0.88–1.49)		
Genital discharge				
No	1		1	
Yes	2.67	(2.11–3.38)	1.47	(1.09–1.99)
Abdominal pain				
No	1			

(Continues)

TABLE 4 | (Continued)

		cOR		aOR ($n=1297$)
Yes	0.98	(0.78–1.24)		
Symptomatic presentation[a]				
No	1			
Yes	2.17	(1.67–2.83)		
VDS/MUS				
No	1			
Yes	3.08	(2.41–3.94)	1.91	(1.39–2.61)

Abbreviations: aOR, adjusted odds ratio; ART, antiretroviral therapy; cOR, crude odds ratio; HTS, HIV testing services; MUS, male urethritis syndrome; OPD, outpatients department; STI, sexually transmitted infection; VDS, vaginal discharge syndrome.
[a]Symptomatic presentation at study entry was defined as clients presenting with any of the following self-reported symptoms, comprising genital itchiness or discharge, pain when urinating or during sex, abdominal pain in women, and scrotal swelling in men.
[b]This category was dropped due to collinearity.

0.99–2.13) and lower for one of the community-based fixed testing sites (aOR 0.62, 0.42–0.93) vs. Nhlangano secondary care facility. A clear trend of decreasing odds was observed for consecutively older age groups when compared to the 18–29 age bracket. The odds were elevated for receiving goods for sex (aOR 1.89, 1.12–3.18) while there was a tendency of lower odds for individuals reporting one sexual partner (aOR 0.62, 0.40–0.96) vs. reporting none. With regard to STI symptoms, the odds were increased for clients reporting pain when urinating (aOR 1.86, 1.39–2.49), genital discharge (aOR 1.47, 1.09–1.99), and being diagnosed with VDS/MUS (aOR 1.91, 1.39–2.61).

4 | Discussion

We demonstrated a substantial high burden of a broad range of STIs in this high HIV burden setting. Combined CT/NG/TV infection was particularly common in vulnerable populations like young people and factory workers, and it was associated with certain risky behaviours such as transactional sex. CT/NG/TV and HSV-2 coinfections raise concerns about sustaining HIV control.

4.1 | Bacterial and Parasitic STIs

The prevalence of individual STIs in our study fell within a comparable range (CT, TV) while there was a potential trend towards higher rates for NG and TP compared to other Sub-Saharan African settings [20–22] including a study from Eswatini (9.7% TP positivity in our study vs. 1.2%) [15], and overall aligns with trends reported in other high HIV-burden settings in sub-Saharan Africa.

Our study showed a higher combined CT/NG/TV burden (31.7%) compared to a previous study in Eswatini. That study targeted sexually active and inactive young people living with HIV, where the overall prevalence was 8.7% and reached 25.0% in women aged 20–24 years [16]. It was comparable to a tertiary hospital setting in Taiwan (30.0%) targeting at-risk people living with HIV [23], but lower in pregnant women accessing an antenatal clinic in Haiti (35.7%) and HIV-positive pregnant women using antenatal care services at two facilities in a township in South Africa (47.8%) [24, 25]. Possible explanations for variations include demographic disparities between study populations, diverse risk behaviours. Other factors may be HIV co-infection, variability across care sites, different study methods, and other unmeasured confounding factors. Importantly, our study comprised outpatient department attendees suspected of STIs via the syndromic approach, constituting 22.9% of the total sample, thus possibly leading to an overrepresentation of individuals with CT/NG/TV infections. In addition, similar to other African settings [26, 27], the COVID-19 pandemic reportedly increased risk behaviour, gender-based violence, and impaired functioning of health services in Eswatini, which may have contributed to the spread of STIs. Finally, the Southern African region is recognised to have the highest burden of curable bacterial/parasitic STIs globally [28].

Moreover, numerous individuals with combined CT/NG/TV infections presented asymptomatic, as also observed in other Sub-Saharan African settings [29, 30]. This suggests the need to screen and test for asymptomatic infections to avert long-term complications [31]. On a population scale, asymptomatic infections could significantly contribute to unrecognised transmission of CT/NG/TV. However, implementation of routine testing for asymptomatic infections at scale demands careful consideration. Its impact on incidence reduction may not be immediately apparent [31], while introducing potential public health risks, such as the development of AMR due to increased antibiotic use. Thus, screening and testing programmes should thoroughly evaluate contextual factors before implementation. These include programmatic reach for specific STIs targeted, the proportion of asymptomatic STIs in the target population, frequency of screening, and algorithms used to guide individuals into screening, as well as the sensitivity of laboratory tests [32–34].

Complicating screening interventions, the use of client self-reported symptom-based screening methods appears ineffective in distinguishing between individuals with and without laboratory-confirmed CT/NG/TV infections. However, innovative predictor risk scores, as suggested for acute and early HIV infection in this and other settings [19, 35–37], incorporating a more comprehensive set of criteria, may provide effective screening pathways. For instance, a risk score from

Eswatini, applied to young people living with HIV, integrated five predictors for CT/NG/TV infection and included leukocyte esterase testing, thereby improving prediction compared to relying solely on syndromic screening [38]. However, risk scores [22, 38] may require validation across diverse populations and settings. They should also be assessed for their practicality in routine care settings and for different pathogen combinations.

4.1.1 | HIV, HSV-2 and CT/NG/TV

The prevalence of HSV-2 infection was high and overall comparable to similar settings in Sub-Saharan Africa [39–41], raising concerns about the intertwined epidemics of HSV-2 and HIV. HSV-2 infection is known to increase the transmission and acquisition of HIV [12–14] and non-ulcerative STIs elevate the risk of HIV transmission through genital shedding of HIV [13, 14].

Despite Eswatini achieving the status of HIV epidemic control, surpassing the UNAIDS 95-95-95 targets for HIV in 2021 [17], HIV incidence and prevalence remained elevated compared to most other countries [42]. Addressing HSV-2 and CT/NG/TV coinfections appears crucial for sustained HIV control. For example, although routine screening for asymptomatic HSV-2 infections is typically not advised (e.g., due to false positive results), it could prove beneficial for individuals with an HSV-2-positive partner, people living with HIV, pregnant women, and those with current or recent STIs engaging in high-risk behaviours [43–45]. Additionally, while STIs care has been incorporated into HIV programming, the integration seems weak [40], often overshadowed by a strong focus on HIV funding by external donors. This raises concerns about sustained HIV epidemic control amid elevated rates of STIs infections [46].

4.1.2 | HPV

The consistently high prevalence of HPV in this and similar settings, coupled with strains carrying an increased risk of development of cervical cancer [47–49], underscores the need for improved screening, quality diagnosis, accessible treatment options, and strain detection to guide the selection of HPV vaccines. This is particularly critical in environments with elevated rates of HIV coinfection, as HIV increases the likelihood of asymptomatic HPV infections to progress to invasive cervical cancer [50]. The integration of basic cervical cancer care into existing health structures and HIV care programmes appears imperative. This has proven to be feasible in this and other settings [51, 52].

4.1.3 | HBV, HCV

The burden of HBV infection aligns with other settings [53–55], whereas HCV infection appears lower [56–58]. The prevalence of HCV infection is likely influenced by contextual factors (e.g., urban vs. rural), distinct behavioural and clinical risk factors and may differ from HBV infection [59–61]. Although both viruses do not significantly interact with other STIs, addressing them as part of a broader STIs package is crucial. With the availability of affordable RDT for HCV and HBV infection, settings with at-risk populations and a higher burden of these hepatic viruses should consider routine screening and testing in addition to antiviral therapy and HBV vaccination.

4.2 | Implications for STIs Programming

The high burden of STIs, especially among vulnerable groups like factory workers, young individuals, those engaged in transactional sex, and individuals using alcohol, highlights multifaceted vulnerabilities. While a self-reported symptom-based screening may be ineffective in guiding individuals to STIs care, focusing on locations frequented by vulnerable groups could be a promising initial programmatic strategy. Specific programmatic strategies could include targeted outreach at high-risk sites, enhanced partner notification services, and scaling up affordable point-of-care diagnostics within decentralised and primary care settings.

In addition, our data, along with local evidence [62–64], suggest the presence of complex concurrent and transactional sexual relationships. Thus, understanding and addressing socioeconomic vulnerabilities and sexual networks, along with strengthening partner notification services [19] appears imperative for successful STIs care programming. The high burden of STIs among young people, their link to risky sexual behaviours (e.g., condomless sex), and the convergence of HIV, other chronic viral STIs, and CT/NG/TV infections highlight the need for action. It is crucial to urgently strengthen the integration of STI, HIV, and reproductive health services across the prevention, diagnostics, and treatment cascade at programme, facility, and consultation levels.

4.3 | Limitations

A main limitation is the purposive sampling of study sites. While it allowed for oversampling specific population groups, thus enhancing our understanding of their STIs exposures, it restricted the generalisability to the broader population of Eswatini. Additionally, clinic-based recruitment did not capture the STI burden in the wider community.

Importantly, the reliance on self-reported sexual behaviour may have introduced recall or social desirability bias, potentially affecting the accuracy of behavioural risk assessments. Supported by other studies [65, 66], our findings also raise concerns about the reliability of patients' self-questionnaires on risky behaviours and risk factors related to STIs, considering that infections with CT/NG/TV were not uncommon among those reporting no sexual intercourse in the prior 6 months.

In addition, the sample size for eligible clients in the analysis was reduced by a database error during data saving, resulting in a loss of 5.9% of the eligible sample. We opted not to include their partial data as a more comprehensive analysis on associations with STIs infection would have been impractical.

Given the limitations of the antibody-based TP lateral flow RDT, we could not definitively distinguish between active and cured syphilis infections. The RPR results suggested very early, late, or undetermined infection duration, or possibly serological scars

from past treatment. Follow-up RPR tests and a comprehensive clinical history are needed to accurately determine the status of TP infection.

A key strength is the simultaneous assessment of a wide range of STIs, providing a comprehensive overview of all preventable, curable, and treatable STIs in a region with a high HIV burden. Many studies typically focus on the main bacterial and viral STIs separately. We offer a comprehensive perspective on the interplay of these STIs in a resource-poor setting in Eswatini, likely applicable to similar settings in Southern Africa.

5 | Conclusions

We found a substantial burden of diverse STIs in Eswatini post COVID-19, compounded by socio-demographic vulnerabilities and exacerbated by behavioural risk factors. Our findings support the integration of STI and HIV care at primary healthcare levels, the expansion of molecular testing beyond pilot settings to improve detection and management, and the strengthening of prevention efforts. Future research should also explore the burden and trends in antimicrobial resistance in bacterial STIs to inform treatment strategies.

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Conflicts of Interest

The authors declare no conflicts of interest.

Data Availability Statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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