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Prevalence of *Chlamydia trachomatis*, *Neisseria gonorrhoeae* and *Mycoplasma genitalium* at pharyngeal and anorectal sites in patients presenting to an STI outpatient ward

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Abstract

Background: The incidence of sexually transmitted infections (STIs) is unbridled and on the rise. Extragenital STIs (anal and pharyngeal infections) are commonly asymptomatic, resulting in delayed diagnosis and treatment and consequently higher chances of onward transmission.

Objective: The aim of this observational single-centre study was to determine the prevalence of STIs at extragenital sites in symptomatic and asymptomatic patients presenting at an STI outpatient clinic.

Methods: We conducted a retrospective analysis of patients who presented between October 2019 and February 2021 at the STI outpatient clinic of a tertiary centre in Central Europe. Patients were included in the study if they received at least one pharyngeal and/or anorectal swab in addition to a genital swab for multiplex-PCR STI diagnostics. Demographic data, symptoms and serological results were collected and analysed.

Results: Data collected from 440 patients were analysed (mean age: 33.9 years, male: $n = 345$, 78.4%, female: $n = 95$, 21.6%). Ninety-seven males reported having sex with men (MSM); 174 patients identified as heterosexual (132 males, 42 females), and 10 females as bisexual. The sexual orientation was not reported in 159 cases. An STI was confirmed in 195 patients (44.3%) and, among those, 109 patients (55.9%) tested positive for an STI at extragenital sites. Seventy-one patients had a pharyngeal STI whereas 61 were infected in the anorectal region. Of those suffering from an extragenital STI, 64.2% (70 out of 109) tested negative for relevant pathogens at genital sites. The most frequently detected extragenital pathogen was *Neisseria gonorrhoeae* (71.8% of all pharyngeal STIs [51 out of 71], 55.7% of anorectal STIs [34 out of 61]), followed by *Chlamydia trachomatis* (41.0% of all anal infections [25 out of 61], 5.6% of pharyngeal infections [4 out of 71]). Pharyngeal and anorectal infections were asymptomatic in 88.7% [63 out of 71] and 65.6% [40 out of 61] of the cases, respectively.

Conclusions: These results underline the need to perform multisite testing, regardless of the presence of symptoms.

A. Kogler and B. Sadoghi contributed equally to this work.

INTRODUCTION

The rising incidence of sexually transmitted infections (STIs) is a major global public health concern that affects millions of people annually.[1,2] If left untreated, STIs can lead to serious sequelae, such as ascending infections, pelvic inflammatory disease, ectopic pregnancy, infertility, as well as neurological and cardiovascular disease.[3] Moreover, STIs can facilitate both the acquisition and transmission of other STIs, including the human immune deficiency virus (HIV).[4] Historically, STIs have been considered primarily a urogenital disease affecting the urethra, vagina and cervix. More attention, however, has recently been directed towards extragenital STIs (eSTIs) in the anorectal and pharyngeal regions.

Herpes simplex viruses 1 and 2 (HSV-1, -2), *Neisseria gonorrhoeae* (NG), *Chlamydia trachomatis* (CT), *Treponema pallidum* (TP) and *Mycoplasma genitalium* (MG) are among the most commonly reported eSTI agents and organisms. These can be transmitted through different types of sexual activity, including oral and anal sex.[2,5–7] While eSTIs may manifest as pharyngitis or proctitis, they often remain asymptomatic.[8] Although the clinical relevance of eSTI transmitters has not yet been fully understood, they are suspected to serve as sources of ongoing transmission and potentially contribute to the increasing incidence of STIs.[6]

As the current data on eSTIs in Austria in an all-comer population is limited, this retrospective study was carried out to evaluate the prevalence of CT, NG and MG at pharyngeal and anorectal sites in individuals presenting to an STI outpatient ward to improve overall knowledge and to establish more effective screening approaches for STIs at extragenital sites.

MATERIALS AND METHODS

This is as a retrospective, single-centre study carried out to estimate the prevalence of eSTIs among individuals presenting at an STI outpatient ward at a tertiary-care centre in Central Europe. We included data collected from patients who were ≥18 years of age and received at least one anal and/or pharyngeal swab between October 2019 and February 2021 at our STI outpatient clinic. Data from transsexual individuals, professional sex workers, and people who were tested or treated at a different healthcare facilities were not included in the analysis. Patients were offered pharyngeal and/or anal swabs based on their sexual orientation, irrespective of the presence of symptoms. Specifically, anal swabs were consistently conducted for all men who have sex with men (MSM), while heterosexual male patients did not routinely undergo anal swab testing. All females were offered anal testing, irrespective of conducting in anal intercourse, due to the close anatomical proximity of the vagina and anus, which facilitates simultaneous transmission and autoinoculation.

Demographic data, clinical symptoms, swab results, serological results and PCR results were retrospectively collected from the medical records. The included patients had been tested for either two (CT/NG) or eleven (CT, NG, HSV-1, HSV-2, *Haemophilus ducreyi* (HD), MG, *Mycoplasma hominis* (MH), TP, *Trichomonas vaginalis* (TV), *Ureaplasma parvum* (UP) and *Ureaplasma urealyticum* (UU) pathogens using a multiplex PCR Array) 'EUROArray'; Euroimmun® (Lübeck, Germany). No samples were pooled, and no samples were self-collected.

We defined the following as relevant STI pathogens: CT, NG, HSV-1, HSV-2, MG and TP. An eSTI was defined as being present if the rectal and/or pharyngeal swab yielded a positive PCR result for at least one of the following pathogens: NG, CT, MG, HSV-1, HSV-2, TV and HD. Every positive pharyngeal test for NG was confirmed by real-time in-house PCR, in order to minimize false-positive results. Serovar analysis for CT subtypes L1, L2 and L3 was routinely performed on MSM with a positive anorectal test for CT, and in those where clinical hints were present, including buboes or proctitis-like symptoms. However, LGV was not included in this study analysis. Positive results for MH, UU or UP were not included in the analysis, as they are considered to be commensal organisms that are commonly found in the anogenital region, and their presence does not typically require treatment.

Statistical analysis

Categorical data were summarized using absolute (number of cases) and relative frequencies (percentages). Continuous data were summarized using medians and interquartile ranges [IQR] or means. To compare the categorical and continuous variables between the study participants, they were divided into two groups based on the PCR confirmation of an eSTI. The 'No eSTI' group consisted of individuals without a confirmed eSTI, while the 'eSTI' group included individuals with a confirmed eSTI.

To assess differences in categorical variables, Pearson's chi-squared test and Fisher's exact test were used. The distribution of continuous variables was evaluated using the Shapiro–Wilk test, indicating that all metric variables were non-parametric. Subsequently, the Mann–Whitney *U*-test for independent samples was used to compare continuous variables between both groups. The effect size (ES) was estimated by calculating Pearson's ρ using the *z* values obtained from the inferential test ($|\rho| = \frac{z}{\sqrt{n}}$, where n represents the total number of cases). An ES of $r = 0.1$ indicates a small effect, $\rho = 0.3$ a medium and $\rho = 0.5$ large effect. All statistical tests were two-tailed, and the level of significance was set to $p < 0.05$.

RESULTS

The study population's baseline characteristics are presented in Table 1. In total, 440 patients were included (male: $n = 375$, 78.4%; female: $n = 95$, 21.6%), with a mean age of

TABLE 1 Demographic characteristics of the study population.

Characteristics	Total (n = 440)	Missing, n (% of total)
Age [years] at enrolment ($n = 440$)		0 (0.0%)
Mean ± SD	33.9 ± 11.6	
Median [IQR]	31 [15.3]	
Gender ($n = 440$)		0 (0.0%)
Female	95 (21.6%)	
Male	345 (78.4%)	
Sexual orientation ($n = 281$)		159 (36.1%)
Heterosexual women	42 (14.9%)	
Heterosexual men	132 (47.0%)	
MSM	97 (34.5%)	
Bisexual women	10 (3.6%)	
Partnership ($n = 366$)		74 (16.8%)
Committed partnership	159 (43.4%)	
Random acquaintance	189 (51.6%)	
Committed and random	18 (4.9%)	
Sex toy usage ($n = 65$)		375 (85.2%)
Yes	21 (32.3%)	
No	44 (67.7%)	
STI in the past ($n = 265$)		175 (39.8%)
Yes	145 (54.7%)	
No	120 (45.3%)	
Meningoccoci vaccination ($n = 53$)		387 (88.0%)
Yes	5 (9.4%)	
No	48 (90.6%)	
HPV vaccination ($n = 69$)		371 (84.3%)
Yes	2 (2.9%)	
No	67 (97.1%)	

Note: The total number of observed cases for each characteristic are indicated in the first column. In the second column, values are presented as absolute and relative frequencies (%) relative to the number of observed values, mean ± standard deviation (SD), or median and interquartile range [IQR]. The IQR is calculated by subtracting the value of the 75th from the value of the 25th percentile. The 'Missing *n* (%)' column indicates the absolute and relative frequency of not reported values, with the percentages calculated relative to the total number of included patients ($N = 440$), for each characteristic.

Abbreviations: HPV, human papilloma virus; MSM, men who have sex with men (including bisexual men); STI, sexually transmitted infection.

34.6 years for men and 31.5 for women. Heterosexuality (61.9% [174 out of 281]) was the most common sexual orientation, followed by those who identified themselves as MSM (34.5% [97 out of 281]) and bisexual women (3.6% [10 out of 281]). For 159 patients (36.1% [159 out of 440]), no documentation about their sexual orientation was available.

The prevalence of CT, NG, HSV-1, HSV-2, HD, MG, MH, TP, TV, UP and UP at any site is presented in Table 2.

Extragenital STIs (eSTIs)

An eSTI could be confirmed in 24.8% [109 out of 440] of all patients, of which 44.0% [48 out of 109] tested positive for a pharyngeal STI and 34.9% [38 out of 109] for an anal STI. In 21.1% [23 out of 109] of the patients, a simultaneous infection at both extragenital sites was verified, and the simultaneous presence of a genital STI could be confirmed in 35.8% [39 out of 109] individuals (Figure 1). A comprehensive visualisation of the site-specific occurrences and the patterns of overlapping infections are illustrated in Figure 2.

Pharyngeal testing was conducted in 418 (95%) of all 440 patients. Of these, 17.0% [71 out of 418] tested positive for a pharyngeal STI. The most common pharyngeal pathogen was NG (71.8% [51 out of 71]), followed by HSV-1 (18.3% [13 out of 71]), TP (9.9% [7 out of 71]), CT (5.6% [4 out of 71]) and MG (1.4% [1 out of 71]). None tested positive for HSV-2. In five patients, a co-infection with two pathogens was present (7.0% [5 out of 71]).

Anal testing was performed in 241 (54.8%) of all 440 individuals, with 25.3% [61 out of 241] representing confirmed anal STI cases. The most common anorectal pathogen was NG (55.7% [34 out of 61]), followed by CT (41.0% [25 out of 61]), TP (6.6% [4 out of 61]), MG (6.6% [4 out of 61]), HSV-2 (4.9% [3 out of 61]) and HSV-1 (1.6% [1 out of 61]). Seven patients (11.5% [7 out of 61]) had a co-infection with two pathogens, and one patient (1.6% [1 out of 61]) with three pathogens.

Symptoms

In total, 303 out of 440 patients (68.8%) presented due to symptoms for STI testing. Only 7.3% [32 out of 303] reported experiencing pharyngeal complaints, and 10.0% [44 out of 303] reported anal complaints. One patient had complaints at both sites (0.2% [1 out of 303]) (Figure 3). The most prevalent pharyngeal symptom was sore throat (71.9% [23 out of 32]), while most patients with anorectal symptoms (79.5% [35 out of 44]) presented with proctitis-like symptoms, including rectal pain, rectal itching, diarrhoea, dyschezia, urgency, tenesmus, blood and/or mucus in their stool.

Regarding the 32 patients with pharyngeal symptoms, 8 had an STI (25.0% [8 out of 32]). Notably, 92.2% [47 out of 51] of those with pharyngeal gonorrhoea and all cases of pharyngeal CT [4 out of 4] infections were asymptomatic. Asymptomatic courses were also common in patients infected with HSV-1 (76.9% [10 out of 13]) and TP (71.4% [5 out of 7]) (Figure 4).

Out of the 44 patients who reported anal symptoms, 21 were tested positive for an STI, representing a prevalence of 47.7%. Within this group, an asymptomatic course was observed in 64.7% [22 out of 34] of anal gonorrhoea cases, and in 80% [20 out of 25] of anal CT infections. Moreover, 75% [3 out of 4] of those infected with TP had

TABLE 2 Prevalence of STIs, by pathogen and anatomical location.

Anatomical site tested	Number of patients with a test result positive for a specific pathogen at a specific body site											
	Any pathogen *n* (%)	CT *n* (%)	NG *n* (%)	HSV-1 *n* (%)	HSV-2 *n* (%)	HD *n* (%)	MG *n* (%)	MH *n* (%)	TP *n* (%)	TV *n* (%)	UP *n* (%)	UU *n* (%)	Multiple pathogens
Pharynx ($n=418$)	99 (23.7%)	4 (1.0%)	51 (12.2%)	13 (3.1%)	0 (0.0%)	0 (0.0%)	1 (0.2%)	15 (3.6%)	7 (1.7%)	12 (2.9%)	8 (1.9%)	8 (1.9%)	20 (4.8%)
Urethra ($n=421$)	220 (52.3%)	50 (11.9%)	40 (9.5%)	8 (1.9%)	8 (1.9%)	0 (0.0%)	22 (5.2%)	33 (7.8%)	11 (2.6%)	1 (0.2%)	79 (18.8%)	63 (15.0%)	95 (22.6%)
Vagina ($n=16$)	13 (81.3%)	2 (12.5%)	2 (12.5%)	0 (0.0%)	1 (6.3%)	0 (0.0%)	0 (0.0%)	5 (31.3%)	0 (0.0%)	1 (6.3%)	8 (50.0%)	4 (25.0%)	10 (62.5%)
Cervix ($n=72$)	47 (65.3%)	7 (9.7%)	8 (11.1%)	1 (1.4%)	2 (2.8%)	0 (0.0%)	4 (5.6%)	11 (15.3%)	0 (0.0%)	0 (0.0%)	36 (50.0%)	6 (8.3%)	28 (38.9%)
Rectum ($n=241$)	80 (33.2%)	25 (10.4%)	34 (14.1%)	1 (0.4%)	3 (1.2%)	0 (0.0%)	4 (1.7%)	19 (7.9%)	4 (1.7%)	1 (0.4%)	8 (3.3%)	15 (6.3%)	34 (14.1%)

no complaints, and half of the MG infections [2 out of 4] were also asymptomatic. In contrast, HSV-2 infections showed a symptomatic course in 66.7% [2 out of 3] of the patients (Figure 5).

The distributions of symptomatic versus asymptomatic patients who tested positive for pharyngeal and anorectal STIs are presented in Figures 4 and 5.

Subgroup analysis of MSM ($n=96$)

Pharyngeal testing was conducted in 87.6% ($n=85$) of all 97 MSM. Among these, 20% [17 out of 85] tested positive for a pharyngeal STI. The most common pharyngeal pathogen was NG 70.6% [12 out of 17], followed by TP (17.6% [3 out of 17]), HSV-1 (11.8% [2 out of 17]), CT (5.9% [1 out of 17]) and MG (5.9% [1 out of 17]). None tested positive for HSV-2. Co-infections involving two pathogens were detected in two patients (11.8% [2 out of 17]).

Anal STI testing was performed in 81.4% ($n=79$) of all MSM, with 21 patients (26.6%) testing positive. The most common anorectal pathogen was NG (57.1% [12 out of 21]), followed by CT (33.3% [7 out of 21]), TP (9.5% [2 out of 21]), MG (4.8% [1 out of 21]) and HSV-2 (4.8% [1 out of 21]). None tested positive for HSV-1. Two patients had a co-infection with two pathogens (9.5% [2 out of 21]).

Comparison: 'No eSTI' versus 'eSTI'

No significant differences were found between the two groups regarding age, duration of symptoms, number of sexual partners within the past 9 months or the lifetime number of sexual partners (Table 3). However, the eSTI group reported a significantly shorter time since their last sexual contact (21 [38] days vs. 12 [23] days, $p=0.010$).

Differences in categorical variables are depicted in Table 4. A greater proportion of eSTI patients reported genital symptoms (59.1% vs. 46.3%, $p=0.020$). Extragenital symptoms were also more prevalent in the eSTI group (27.8% vs. 13.7%, $p=0.001$), with a significantly higher proportion of eSTI patients reporting anorectal symptoms (20.4% vs. 6.7%, $p<0.001$). Additionally, a significant relationship was observed between sexual orientation and the presence or absence of eSTI ($p<0.001$): More MSM (56.1% vs. 27.9%) and bisexual women (7.6% vs. 2.3%) were identified as eSTI patients, while heterosexuality was more common among patients without an eSTI (69.8% vs. 36.4%).

DISCUSSION

This retrospective analysis enabled us to investigate the prevalence of extragenital STIs (eSTIs) in a large sample of an all-comer population presenting to a tertiary academic centre's STI outpatient ward in Central Europe. The study's most important finding is that more than half of

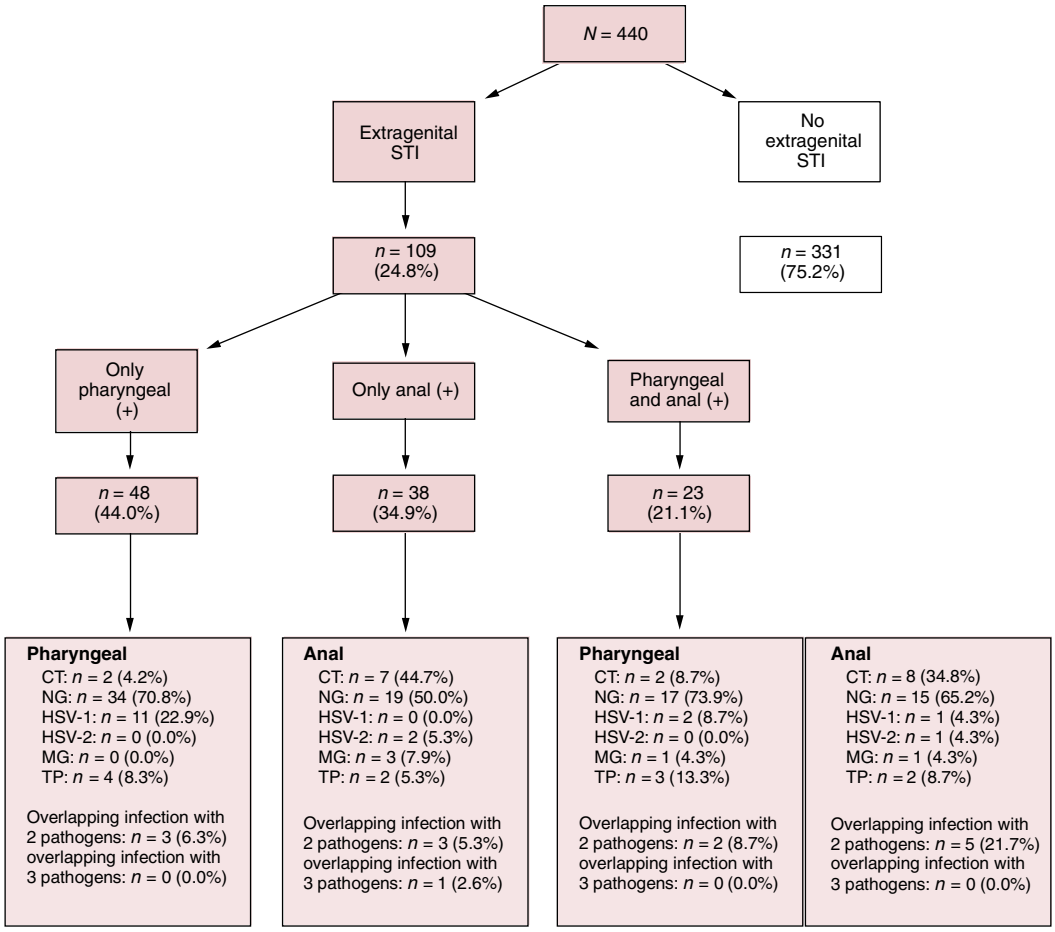

FIGURE 1 Flowchart of the STI screening results with emphasis on extragenital STIs.

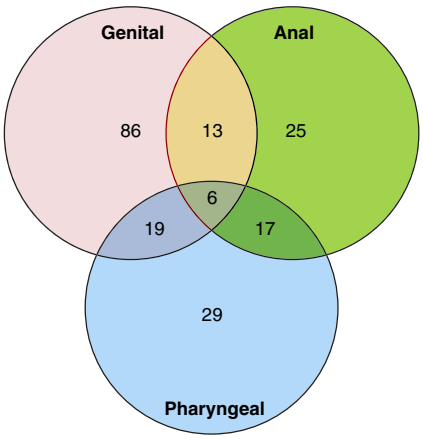

FIGURE 2 Venn diagram illustrating the distribution of STI pathogens among the pharyngeal (total number of infections: $n = 71$), anal (total number of infections: $n = 61$) and genital sites (total number of infections: $n = 124$), along with the concurrent occurrences of overlapping infections at these locations (pharyngeal: 42 instances of overlapping infections; anal: 36 instances of overlapping infections; genital: 38 instances of overlapping infections) in 440 patients.

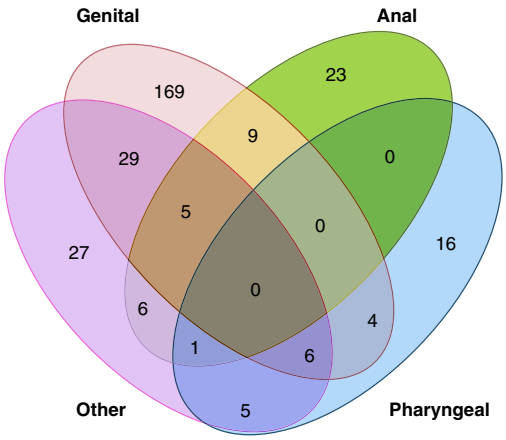

FIGURE 3 Venn diagram illustrating the distribution of symptoms among 303 patients who presented to our STI outpatient ward due to the presence of symptoms: genital (total number of patients: 222), anal (total number of patients: 44), pharyngeal (total number of patients: 32) and other symptoms (total number of patients: 79), highlighting concurrent overlapping symptoms.

all confirmed STIs were located at extragenital (pharyngeal and/or anorectal) sites, with most infected individuals following an asymptomatic course. Within our cohort, patients with pharyngeal STIs rarely presented with symptoms (11.3%), whereas individuals consulting the STI clinic due to pharyngeal symptoms did not suffer from an STI in most cases. Regarding anal STIs, about one-third of patients that suffered from an anal STI reported complaints (34.4%), and nearly half of the patients with anal symptoms tested positive for an anal STI.

In 2016 Chan et al. published a comprehensive literature review encompassing 80 studies examining the extragenital prevalence of NG and CT, which varied by gender and sexual orientation.[6] Regarding pharyngeal NG infections, they reported a prevalence ranging from 0% to 29.6% in females, 0.5% to 16.5% in MSM and 0.4% to 15.5% in heterosexual men.[6] These data are comparable to our findings, as we identified a corresponding prevalence of 11.6% in women, 17.0% in MSM and 5.4% in heterosexual men. Regarding anorectal NG infections, Chan et al. reported a prevalence ranging from 0.6% to 35.8% in females, 0.2% to 24% in MSM and 0.5% to 7% in heterosexual men.[6] Our findings fit within this range, with anal NG infections being confirmed in 13.8% of females and 17.2% of MSM. Comparing site-specific NG infection, addressed in a retrospective cross-sectional study by Valejo et al.[9] who examined extragenital NG infections among 1798 MSM, we observed a lower percentage of anorectal-only NG infections (21.4% vs. 57%), higher rates of oropharyngeal-only NG-infections (37.1% vs. 10%) and a greater proportion of cases with both extragenital and urogenital NG infections (27.1% vs. 18%).

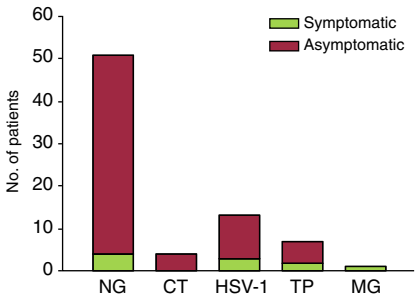

FIGURE 4 Stacked column chart illustrating the distribution of symptomatic versus asymptomatic patients who tested positive for pharyngeal STIs (total number of patients: $n = 71$).

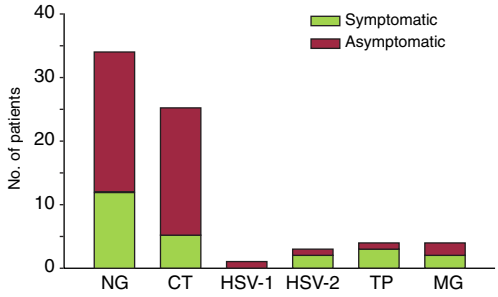

FIGURE 5 Stacked column chart illustrating the distribution of symptomatic versus asymptomatic patients who tested positive for anorectal STIs (total number of patients: $n = 61$).

The high prevalence of pharyngeal NG infections is concerning owing to their potential to serve as a reservoir for antimicrobial NG resistance development.[10] This underscores the need for regular screening for oropharyngeal NG, especially considering the fact that many of these infections follow an asymptomatic course. For instance, in Valejo et al.'s study on MSM, only 14% of confirmed oropharyngeal infections showed infection-related symptoms.[9] Similarly, we found that 92.2% of pharyngeal NG infections were asymptomatic, aligning with results from a retrospective study by Peters et al., where 93% of females with pharyngeal infections showed no symptoms[7] and Richardson et al.[11] who reported symptoms in only 7%.[11] Concerning anorectal NG infections and related symptoms, Peters et al.,[7] found that all 15 examined females (100%) with anorectal NG infections were asymptomatic in their study. This contrasts with findings reported by Valejo et al.[9]; in their study, symptoms potentially associated with NG infections were observed in 52% (38 out of 73) of confirmed anorectal NG infections. In comparison, we found that 56.5% of all men (all MSM) with verified anal NG infections and 81.8% of all women (irrespective of their sexual orientation) with confirmed anorectal NG

TABLE 3 Comparison of non-parametric continuous variables between the 'No eSTI' and 'eSTI' groups using Mann–Whitney *U*-test for independent samples.

	No eSTI (total $n = 331$)			eSTI (total $n = 109$)				
	n	Missing n (%)	Mdn [IQR]	n	Missing n (%)	Mdn [IQR]	ES |r|	p
Age (years)	331	0 (0.0%)	30 [15]	109	0 (0.0%)	31 [16]	0.03	0.552
Duration of symptoms (days)	274	57 (17.2%)	6.5 [26]	96	13 (11.9%)	3.5 [18]	0.06	0.228
Last sexual contact (days)	193	138 (41.7%)	21 [38]	70	39 (35.8%)	12 [23]	0.16	**0.010**
Sexual partners within the last 9 months	114	217 (65.6%)	2 [2]	39	70 (64.2%)	2 [3]	0.00	0.988
Lifetime number of sexual partners	44	287 (86.7%)	12 [25]	15	94 (86.2%)	25 [35]	0.16	0.232

Note: Values represent total number of observed cases (n), absolute and relative frequencies of missing cases ('missing, n (%)' column) with percentages calculated relative to the total sample size for each group, or medians (Mdn) and interquartile ranges [IQR]. Significant p values ($p < 0.05$) are shown in bold.

Abbreviations: ES, effect size using Pearson's ρ; Mdn [IQR], median (interquartile range).

TABLE 4 Comparison of categorical variables between the 'No eSTI' and 'eSTI' groups.

	No eSTI *n* (%[a])	eSTI *n* (%[a])	*p*
Gender (*n* = 440)			0.231
Male	264 (79.8%)	81 (74.3%)	
Female	67 (20.2%)	28 (25.7%)	
Clinical symptoms (*n* = 438)			0.515
No	99 (30.0%)	36 (33.3%)	
Yes	231 (70.0%)	72 (66.7%)	
Genital symptoms (*n* = 436)			**0.020**
No	152 (46.3%)	64 (59.1%)	
Yes	176 (53.7%)	44 (40.7%)	
Urogenital discharge (*n* = 436)			0.988
No	264 (80.5%)	87 (80.6%)	
Yes	64 (19.5%)	21 (19.4%)	
Dysuria (*n* = 434)			0.374
No	230 (70.6%)	81 (75.0%)	
Yes	96 (29.4%)	27 (25.0%)	
Genital itching (*n* = 436)			0.220
No	290 (88.4%)	100 (92.6%)	
Yes	38 (11.6%)	8 (7.4%)	
Any open sore (*n* = 436)			0.158
No	303 (92.4%)	95 (88.0%)	
Yes	25 (7.6%)	13 (12.0%)	
Open genital sore (*n* = 436)			0.388
No	311 (94.8%)	100 (92.6%)	
Yes	17 (5.2%)	8 (7.4%)	
Open oral sore (*n* = 436)			0.601
No	325 (99.1%)	106 (98.1%)	
Yes	3 (0.9%)	2 (1.9%)	
Open anal sore (*n* = 436)			0.073
No	323 (98.5%)	103 (95.4%)	
Yes	5 (1.5%)	5 (4.6%)	
Extragenital symptoms (*n* = 436)			**0.001**
No	283 (86.3%)	78 (72.2%)	
Yes	45 (13.7%)	30 (27.8%)	
Oropharyngeal symptoms (*n* = 436)			0.648
No	305 (93.0%)	99 (91.7%)	
Yes	23 (7.0%)	9 (8.3%)	
Sore throat (*n* = 436)			0.518
No	312 (95.1%)	101 (93.5%)	
Yes	16 (4.9%)	7 (6.5%)	
Anorectal symptoms (*n* = 436)			**< 0.001**
No	306 (93.3%)	86 (79.6%)	
Yes	22 (6.7%)	22 (20.4%)	
Partnership (*n* = 366)			0.328
Committed partnership	122 (44.0%)	37 (41.6%)	
Random acquaintance	144 (52.0%)	45 (50.6%)	
Committed and random	11 (4.0%)	7 (7.9%)	
Sexual orientation (*n* = 289)			**< 0.001**
Heterosexual	150 (69.8%)	24 (36.4%)	
MSM	60 (27.9%)	37 (56.1%)	
Bisexual women	5 (2.3%)	5 (7.6%)	
Sex toy usage (*n* = 65)			0.757
No	31 (68.9%)	13 (65.0%)	
Yes	14 (31.1%)	7 (35.0%)	
STI in the past (*n* = 265)			0.067
No	94 (48.7%)	26 (36.1%)	
Yes	99 (51.3%)	46 (63.9%)	
Meningococci vaccination (*n* = 53)			0.632
No	34 (91.9%)	14 (87.5%)	
Yes	3 (8.1%)	2 (12.5%)	
HPV vaccination (*n* = 69)			1.000
No	48 (96.0%)	19 (100.0%)	
Yes	2 (4.0%)	0 (0.0%)	

Note: In the first column, the total number of observed cases is indicated for each parameter. Values are presented as absolute (total number of individuals for each observed parameter) and relative frequencies (%). Pearson's chi-squared test and Fisher's exact test were used for inferential statistics, with a $p < 0.05$ indicating a statistically significant difference in column proportions (in bold). Abbreviations: eSTI, extragenital sexually transmitted infection; MSM, men who have sex with men (including bisexual men).

[a]Percentages represent the column percentage based on the respective group.

infections in our study did not report any complaints. These results highlight the importance of anorectal STI testing in asymptomatic women.

Bristow et al. examined 417 patients for extragenital CT infections and did not detect pharyngeal CT infections.[12] A comparably low prevalence of pharyngeal CT infections has been shown in other studies,[13,14] with Bancalari et al. reporting a prevalence of only 6% in a cohort of 200 pregnant adolescent women.[15] Our results match these findings, as we had a low prevalence of pharyngeal CT infections (1.0% of pharyngeal swabs). Regarding anorectal CT infections, one meta-analysis found an average CT prevalence of 9%,[16] findings that are similar to our observed prevalence of 10.4%. However, Bancalari et al. reported a higher rectal CT prevalence (23%), despite less than 5% of participants reported a history of receptive anal intercourse.[15] This can be explained by the anatomical proximity of the vagina and the anus, which allows for concurrent transmission and autoinoculation.

With respect to pharyngeal CT-related symptoms, Peters et al. observed no symptoms in a total of 71 examined females suffering from pharyngeal CT infections.[7] Likewise, all our pharyngeal CT infected individuals were asymptomatic. And finally, regarding anorectal CT-associated complaints, Chan et al. stated that a large proportion of rectal CT infections in females follow an asymptomatic course, with prevalence estimates ranging from 36% to 100%. Similarly, our results show that 80.0% of patients with confirmed anal CT infections

experienced an asymptomatic course (50% were females). Nonetheless, it must be kept in mind that spontaneous partly substantial clearance has been described for CT infections at any site previously.[17] Van Liere et al. described clearance rates for CT infections as ranging from 6.8% (vaginal site) to 12.7% (anorectal site) and even to 57.1% (oropharyngeal site).[17]

In a recent multicentre cross-sectional study, Jansen et al. examined the prevalence of CT, MG, NG and TV in MSM.[14] As compared to previous studies, the authors found one of the highest reported MG prevalence in MSM (17.0%).[14] Furthermore, they observed the highest MG prevalence in the anal region (11.5%), followed by the urethral (5.4%), and pharyngeal regions (2.9%).[14] Our data confirm the presence of MG in 5.3% of urethral swabs, 3.8% of anorectal swabs and 0.5% of oropharyngeal swabs. Among the patients with anal MG infections, two out of four (50.0%) were asymptomatic, while the patient with a pharyngeal MG infection also did not experience any symptoms, and screening for MG at the pharyngeal region is not routinely recommended.

In our cohort, 6.3% of patients tested positive for pharyngeal HSV-1 based on the PCR results, but no cases of oropharyngeal HSV-2 were detected. This finding is consistent with those of previous studies which indicated that HSV-2 is a rarer cause of oropharyngeal herpes infections.[18,19] Of the patients who tested positive for oropharyngeal HSV-1, only about a quarter (23.1%) presented with oropharyngeal symptoms, with one case diagnosed as co-infected with TP. This is likely due to the high rate of asymptomatic viral shedding which is typical for HSV infections.[20,21] Additionally, 37% of patients with pharyngeal symptoms tested positive for HSV-1; this result is not uncommon, as HSV-1 is a well-known pathogen in those suffering from pharyngitis.[22] It must be discussed that HSV-1 at the oropharyngeal region might not only be attributed to sexual contact; positive PCR results might also stem from viral shedding and/or auto-infection from an active herpes labialis. However, clinically, an active herpes labialis has not been documented in those patients who tested positive. Anorectal HSV infections were only prevalent in 1.0% of confirmed HSV-1 and 2.9% of HSV-2 patients. Among patients with anorectal HSV-2 infections, two-thirds (2 out of 3) showed symptoms; however, one patient had a co-infection with NG.

Yang et al. reported a remarkably high detection rate of TP in oral swabs from MSM with oral ulcers (40%).[23] In our cohort, only two patients exhibited clinical pathogenic lesions linked to syphilis, but the PCR was positive for TP in seven patients, all of whom were serologically confirmed to have syphilis. Furthermore, in the study by *Towns* et al., among patients who tested positive for TP DNA in oral swabs, half of them (24 out of 48) had no oral lesions, suggesting that clinically asymptomatic TP shedding from the mouth and anus may contribute to the ongoing transmission of syphilis among MSM.[24] Notably, it has been demonstrated that oral detection of TP in MSM during the secondary stage of syphilis was highest as compared to other stages, highlighting the potential role of oral transmission even without clinical manifestations of TP infection.[24]

Regarding anal TP infections, Towns et al. examined MSM with untreated early syphilis and found anal TP in 45 out of 196 men (23%).[24] This prevalence is remarkably higher than our observed overall prevalence of anal TP infections (3.8%). Moreover, Towns et al. reported no clinically detectable anal lesions in 22% ($n = 10$) of their patients.[24] In comparison, 75% of the serologically confirmed early syphilis patients reported anal symptoms in our study.

Limitations

The first limitation is the retrospective study design, including potential selection bias. Second, the study was conducted at a single tertiary academic centre, which may limit the generalisability of the findings to other populations or settings. Moreover, not all medical records provided information about the patients' sexual orientation, hindering our ability to fully compare our findings with those of other studies that may have included a more diverse range of participants. Finally, important aspects such as condom use, engaging in 'chem-sex', as well as PrEP and PEP, were not specifically addressed or captured in our data, limiting the comprehensive assessment of these variables.

CONCLUSIONS

Our findings highlight the importance of extragenital STI (eSTI) testing, regardless of the presence of symptoms, as the vast majority of patients with eSTIs in our study were asymptomatic (69.1%). Additionally, urogenital STIs were detected in just under one-third of eSTI patients. If we had relied solely on symptom-based testing for pharyngeal and anal STIs, 88.7% of pharyngeal and 66.1% of anal STIs would have remained undetected.

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CONFLICT OF INTEREST STATEMENT

None of the contributing authors have any conflicts of interest, including specific financial interests, relationships and affiliations relevant to the subject matter or materials discussed in the manuscript.

DATA AVAILABILITY STATEMENT

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

ETHICAL APPROVAL

The study was approved by the local institutional review board (IRB) under reference number 33-364 ex 20/21.

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