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Low prevalence of methicillin-resistant *Staphylococcus aureus* among men who have sex with men attending an STI clinic in Amsterdam: a cross-sectional study

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ABSTRACT

Objective: Community-associated methicillin-resistant *Staphylococcus aureus* (CA-MRSA) is common among men who have sex with men (MSM) in the USA. It is unknown whether this is also the case in Amsterdam, the Netherlands.

Design: Cross-sectional study.

Setting: Sexually transmitted infection outpatient low-threshold clinic, Amsterdam, the Netherlands.

Participants: Between October 2008 and April 2010, a total of 211 men were included, in two groups: (1) 74 MSM with clinical signs of a skin or soft tissue infection (symptomatic group) and (2) 137 MSM without clinical signs of such infections (asymptomatic group).

Primary outcome measures: *S aureus* and MRSA infection and/or colonisation. Swabs were collected from the anterior nasal cavity, throat, perineum, penile glans and, if present, from infected skin lesions. Culture for *S aureus* was carried out on blood agar plates and for MRSA on selective chromagar plates after enrichment in broth. If MRSA was found, the spa-gene was sequenced.

Secondary outcome measures: Associated demographic characteristics, medical history, risk factors for colonisation with *S aureus* and high-risk sexual behaviour were collected through a self-completed questionnaire.

Results: The prevalence of *S aureus* colonisation in the nares was 37%, the pharynx 11%, the perianal region 12%, the glans penis 10% and in skin lesions 40%. In multivariable analysis adjusting for age, anogenital *S aureus* colonisation was significantly associated with the symptomatic group (p=0.01) and marginally with HIV (p=0.06). MRSA was diagnosed in two cases: prevalence 0.9% (95% CI 0.1% to 3.4%)). Neither had CA-MRSA strains.

Conclusions: CA-MRSA among MSM in Amsterdam is rare. Genital colonisation of *S aureus* is not associated with high-risk sexual behaviour.

ARTICLE SUMMARY

Article focus

- Community-associated methicillin-resistant *Staphylococcus aureus* (CA-MRSA) is common among men who have sex with men (MSM) in the USA.
- It is unknown whether this is also the case in Amsterdam, the Netherlands.
- In a cross-sectional study at the sexually transmitted infection (STI) outpatient low-threshold clinic, Amsterdam, the Netherlands, we studied the prevalence of *S aureus* and MRSA colonisation and infections among symptomatic and asymptomatic MSM.

Key messages

- Among MSM visiting the STI clinic in Amsterdam CA-MRSA is rare.
- Genital colonisation of *S aureus* is not associated with high-risk sexual behaviour.

Strengths and limitations of this study

- The conclusions are based on systematically collected and aggregated data. The study was limited to the Amsterdam MSM population visiting the STI outpatient clinic.

INTRODUCTION

Staphylococcus aureus is a pathogen that can cause skin and soft tissue infections. Nasal carriage plays an important role in the epidemiology and pathogenesis of this infection.[1 2] Around 20% (range 12–30%) of individuals are persistent *S aureus* nasal carriers, approximately 30% (range 16–70%) are intermittent carriers and about 50% (range 16–69%) are non-carriers.[1 3] A causal relation between *S aureus* nasal carriage and infection is supported by the fact that often the nasal *S aureus* strain and the

infecting strain are the same phage type or genotype.[4] Local antibiotic treatment of *S aureus* from the nares results in the subsequent disappearance of *S aureus* from other parts of the body.[1 2 4–6] Extranasal sites that typically harbour the organism include the skin, perineum and pharynx.[7 8]

Most strains of *S aureus* are methicillin-susceptible *S aureus* (MSSA), but some strains, called methicillin-resistant *S aureus* (MRSA), are resistant to methicillin and all β-lactam antibiotics with the exception of the novel cephalosporin, ceftaroline, that can bind to penicillin-binding protein (PBP2a). MRSA has become a major nosocomial infection control problem (known as healthcare-associated MRSA, or HA-MRSA) in many parts of the world[9] with the exception of the Netherlands and of Scandinavian countries.[10 11] Later on, independent from healthcare institutions, MRSA emerged outside healthcare institutions, like the community-associated (CA-MRSA)[12 13] and livestock-associated (LA-MRSA) infections.[14 15] Resistance to methicillin and other β-lactams in *S aureus* is based on an additional PBP which is coded by a mec gene such as mecA.[8] Homologues of mecA such as mecC were described recently.[15]

CA-MRSA is distinguished from HA-MRSA by clinical, laboratory and epidemiological characteristics.[16] A new CA-MRSA clone (USA300) has been described and was identified in several communities in the USA and Canada.[17–19] New clones of CA-MRSA have also been reported in Europe.[15 17] CA-MRSA often produces Panton-Valentine leukocidin (PVL), a toxin that causes polymorphonuclear leucocyte lysis and tissue necrosis.[17 18]

In men who have sex with men (MSM), outbreaks of CA-MRSA skin infections have been reported and the majority of the patients were HIV infected.[8 19–22] It has been suggested that CA-MRSA might be transmitted in this population from skin to skin during sexual contact.[21 22]

A cross-sectional study among 104 men conducted in Italy did not detect a single case of colonisation with CA-MRSA in HIV-infected MSM.[23] No other study in Europe has reported the prevalence of CA-MRSA colonisation in MSM. The purpose of this investigation was to evaluate the prevalence of, and sexual risk factors for *S aureus* colonisation (MSSA and MRSA) and CA-MRSA infection among MSM visiting the sexually transmitted infection (STI) outpatient clinic in Amsterdam.

METHODS

Study population

Consecutive MSM attending the STI outpatient clinic in Amsterdam, the Netherlands, were invited to participate in this cross-sectional study. We aimed to include both symptomatic men (those who had clinical signs of a skin or soft tissue infection (pustules, abscesses, ulcerations, erythematous painful papules or plaques)) and asymptomatic men (those without aforementioned clinical signs). All participants were asked to complete a questionnaire concerning hospital admissions during the past year, factors known to be associated with *S aureus* colonisation (eg, sharing razor blades and tending animals), STI risk factors and sexual behaviour. STI risk factors were also obtained from the electronic files of the routine patient history.

Swabs were taken from the anterior nasal cavity, throat, perianal area and penile glans. From symptomatic men swabs from suspected infected skin lesions were also obtained. If MRSA was detected, the participant was referred to his general practitioner for an eradication therapy, and the sexual partners of the patient were invited for MRSA screening. The study was approved by the ethics committee of the Academic Medical Center of the University of Amsterdam. All participants provided written informed consent.

Laboratory tests

Culture for *S aureus* was carried out on blood agar plates and for MRSA on selective chromagar plates after enrichment in broth. *S aureus* strains were confirmed by the SA442 (Martineau) nucleic acid amplification test (NAAT) and MRSA strains by the mecA NAAT.[24 25] If MRSA was found, the spa-gene was sequenced as described before.[26]

Statistical analysis

A sample size calculation was carried out prior to the study. The prevalence of MRSA carriage in the general population was estimated to be 0.03%.[24] We aimed to assess whether the MRSA prevalence among MSM patients of the STI clinic was at least 3%. To reject the null hypothesis (prevalence of 0.03% or less among the studied group) with a study power of 95% and a significance level of 0.05, a sample size of at least 113 asymptomatic men was needed; this was rounded up to 125. As men with signs suggestive of *S aureus* skin or soft tissue infection were thought to be more likely to be infected with MRSA, we also aimed to include a group of 75 symptomatic men. Because the expected number of asymptomatic men was much larger than that of symptomatic patients, the inclusion period for the symptomatic participants was scheduled to be longer.

The electronic patient file with routine STI screening data, the questionnaire and the laboratory results were merged into one database. The χ^2 test or Fisher's exact test were used to compare categorical variables between groups; the rank sum test was used to compare continuous variables between groups. Data analyses were performed with STATA software (STATA Intercooled, College Station, Texas, USA), V.11.0. p Values of less than 0.05 were considered statistically significant. Associations between possible risk factors and anogenital *S aureus* colonisation were examined with multivariable logistic regressions, reporting adjusted OR with 95% CI. An initial model included all variables that were significant in bivariable analyses; variables were dropped one

by one from the model based on the likelihood ratio test (if p>0.05); HIV was forced into the model.

RESULTS

In total 214 men were included, starting November 2008. The inclusion of asymptomatic men was completed in December 2008 and of symptomatic men in April 2010. From three participants laboratory results were not available and these were excluded, leaving 211 MSM for the analysis (137 asymptomatic and 74 symptomatic participants). The median age of men in the two groups was similar (38 and 41 years, respectively, p=0.32, see table 1). Men in the two groups were comparable regarding most non-sexual risk factors, sexual risk factors and STI diagnoses, but symptomatic men were more often found to be HIV infected (53% vs 31%; p=0.002) and were more often diagnosed with syphilis (12% vs 1%; p<0.001). Also, use of some drugs (cannabis, cocaine and methamphetamine) was significantly more common in the symptomatic group.

The prevalence of *S aureus* colonisation (including MSSA and MRSA) was 37% (78/211) in the nose, 11% (23/211) in the throat, 12% (26/210) in the perineum and 10% (22/211) on the glans penis. The prevalences were similar between symptomatic and asymptomatic men for nose and throat, but the symptomatic group had significantly higher penile and perineal colonisation prevalences (table 1). In the symptomatic group 40% (27/67) of men had an *S aureus*-infected skin lesion. In one symptomatic and one asymptomatic case MRSA was detected, giving an overall prevalence of MRSA carriage of 0.9% (95% binomial exact CI (95% CI) 0.1% to 3.4%), and a prevalence of 0.7% (95% CI 0.02% to 4.0%) among asymptomatic MSM. Details of these two cases are described in the following. Neither known CA-MRSA nor PVL toxin-producing clones were detected.

S aureus colonisation of the anogenital area (based on penile and perianal swabs) was found in 18% (38/211) of the participants. Participants with and without anogenital *S aureus* colonisation were similar in respect to sexual risk behaviour, drug use, history or diagnosis of sexually transmitted diseases, antibiotic exposure, circumcision status and hygiene behaviour, but men with anogenital *S aureus* colonisation were older (42 vs 38 years; p=0.05), and they were more often HIV infected (58% vs 34%, p=0.007; see table 2). In a multivariable logistic regression analysis, adjusting for age, HIV status (adjusted OR, aOR 2.2, 95% CI 0.96 to 4.9), belonging to the symptomatic group (aOR=2.7, 95% CI 1.2 to 5.9) and having had few sexual partners (aOR 3.1, 95% CI 1.2 to 8.3 for those with <5 sexual partners in the previous year compared to those with over 20 sexual partners) were independently and significantly associated with anogenital *S aureus* colonisation.

We examined associations between nasal carriage of *S aureus* and a long list of possible non-sexual risk factors, like admissions, operations, employment in healthcare sector, shaving habits, participation in team sports, sauna visits and other factors; none of these was associated with *S aureus* colonisation of the nose.

Asymptomatic carrier of MRSA

An HIV-infected 40-year-old, asymptomatic, Dutch MSM was positive for MRSA at the perineum. The MRSA had spa-type t064 and was resistant to ciprofloxacin, gentamicin, oxacillin, penicillin and trimethoprim/sulfamethoxazole. Further genetic analysis revealed mecA+ and Martineau+; pUSA03 and PVL were both negative. Recently, the patient was diagnosed with a hepatitis C infection. In the preceding year he had been hospitalised for an elective operation. He had travelled abroad frequently, including to the USA. He regularly used recreational drugs and visited a public gym and sauna. Furthermore, he engaged in high-risk sex, including unprotected anal intercourse, active and passive fisting, group sex, sex at sex parties and sex with partners met through the internet. We attempted to trace six of his sexual partners of whom four were screened. None had MRSA and none had clinical signs of a skin infection.

Symptomatic carrier of MRSA

In an HIV-infected, 46-year-old Dutch MSM, MRSA was detected on swabs taken from a penile ulcer, the nasal cavity, the perineum and the glans penis. The MRSA had spa-type t002 and was resistant to ciprofloxacin, erythromycin, oxacillin and penicillin. Further genetic analysis revealed mecA+ and Martineau+; pUSA03 and PVL were both negative. In the preceding year the patient had neither been hospitalised, nor operated upon, nor had he travelled abroad. He did not use recreational drugs, and did not visit public gyms or saunas. He had not engaged in high-risk sex; he had had sex with one partner in the preceding year. This partner could not be traced for further screening.

DISCUSSION

The prevalence of MRSA among MSM clients of the STI outpatient clinic in Amsterdam was 0.9% (95% CI 0.1% to 3.4%); among clients without skin lesions this was 0.7% (95% CI 0.02% to 4.0%). This is similar to the overall prevalence in Dutch hospitals (1.8%).[11] No CA-MRSA-associated clones were found in this population. These findings are in contrast to reports from the USA where considerable CA-MRSA prevalences were observed among MSM attending STI screening sites.[21 27] Although some MSM residing in Amsterdam frequently travel to the North American continent, this has not resulted in an extensive introduction of CA-MRSA within the Amsterdam population yet. The low MRSA prevalence among the Dutch population in general and among the MSM STI clinic population may be attributed to the strict Dutch search-and-destroy policy and restrictive antibiotic prescription policy.[10] At present, there is

Table 1 Demographic, behavioural and clinical characteristics, and *S aureus* colonisation of five anatomical locations, of 211 MSM attending the STI clinic, Amsterdam, 2008–1010, according to symptomatology of skin or soft tissue infection

	Asymptomatic N=137		Symptomatic N=74		
Characteristic	**N**	**Per cent**	**N**	**Per cent**	**p Value**
(A) Demographics					
Median age in years (IQR)	38 (31–45)		41 (31–48)		0.32
Dutch ethnicity	111	81.0	54	73.0	0.18
(B) Recreational drugs use					
None	21	15.3	7	9.5	0.23
Alcohol	92	67.2	47	63.5	0.60
Cannabis	34	24.8	33	44.6	0.003
XTC	40	29.2	27	36.5	0.28
GHB	36	26.3	25	33.8	0.25
Poppers (alkyl nitrites)	76	55.5	44	59.5	0.58
Cocaine	29	21.2	27	36.5	0.02
Ketamine	14	10.2	13	17.6	0.13
Amphetamine	8	5.8	7	9.5	0.33
Methamphetamine	3	2.2	6	8.1	0.04
(C) Sexual history					
Number of sexual partners*					0.77
0	19	13.8	9	12.2	
1–4	30	21.9	14	18.9	
5–9	20	14.6	11	14.9	
10–19	28	20.4	15	20.3	
20–39	26	19.0	12	16.2	
40 or more	14	10.2	13	17.6	
Active anal sex with condom†	98	71.5	48	64.9	0.32
Passive anal sex with condom†	79	57.7	58	78.4	0.003
Active anal sex without condom†	68	49.6	32	43.2	0.38
Passive anal sex without condom†	56	40.9	37	50.0	0.20
Active fisting†	21	15.3	15	20.3	0.36
Passive fisting†	14	10.2	11	14.9	0.32
Had group sex*	60	43.8	38	51.4	0.29
Visited a sex club*	85	62.0	47	63.5	0.83
Visited a sex party*	31	22.6	17	23.0	0.95
Met sex partner through internet*	75	54.7	45	60.8	0.40
Had sex abroad*	79	57.7	45	60.8	0.66
(D) STI: history and diagnoses					
History of STI	34	24.8	24	32.4	0.24
HIV infected‡	42	30.9	38	52.8	0.002
Syphilis diagnosis	1	0.7	9	12.2	<0.001
Gonorrhoea diagnosis	9	6.6	5	5.4	0.74
Chlamydia diagnosis	23	16.8	14	18.9	0.70
(E) *S aureus* colonisation					
Nares	50	36.5	28	37.8	0.85
Pharynx	13	9.5	10	13.5	0.37
Perineum	9	6.6	17	23.3	<0.001
Glans penis	10	7.3	12	6.2	0.043
Other locations§	—	—	27	40.3	—

*During the previous year.
†In the past 6 months.
‡HIV status missing for three patients who did not want to be tested.
§Data available from 67/74 only.
GHB, γ-hydroxybutyric acid; MSM: men who have sex with men; *S aureus*, *Staphylococcus aureus*; STI, sexually transmitted infection; XTC, MDMA/methamphetamine.

no indication for routine screening of MSM STI clinic visitors for CA-MRSA in the Netherlands.

We observed similar prevalences of *S aureus* nasal colonisation (37%) in MSM as observed in the general population.[1] Genital *S aureus* colonisation was associated with HIV infection; although HIV infection may be considered a proxy for high-risk sexual behaviour, other markers for risk behaviour were not significantly associated with

Table 2 Demographic, behavioural and clinical characteristics of 211 MSM attending the STI clinic in Amsterdam, 2008–10, by *S aureus* anogenital colonisation status

	S aureus negative N=173		*S aureus* positive N=38		
	N	Per cent	N	Per cent	p Value
(A) Demographics					
Median age in years (IQR)	38 (30–45)		42 (35–49)		0.05
Dutch ethnicity	138	79.8	27	71.1	0.24
(B) Recreational drug use					
None	21	12.1	7	18.4	0.30
Alcohol	118	68.2	21	55.3	0.13
Cannabis	57	33.0	10	26.3	0.43
XTC	53	30.6	14	36.8	0.46
GHB	49	28.3	12	31.6	0.69
Poppers	96	55.5	24	63.2	0.39
Cocaine	44	25.4	12	31.6	0.44
Ketamine	23	13.3	4	10.5	0.64
Amphetamine	12	6.9	3	7.9	0.84
Methamphetamine	7	4.1	2	5.3	0.74
(C) Sexual history					
Number of sexual partners*					0.08
0	18	10.4	10	26.3	
1–4	35	20.2	9	23.7	
5–9	29	16.8	2	5.3	
10–19	35	20.2	8	21.1	
20–39	33	19.1	5	13.2	
40 or more	23	13.3	4	10.5	
Active anal sex with condom†	121	69.9	25	65.8	0.62
Passive anal sex with condom†	110	63.6	27	71.1	0.38
Active anal sex without condom†	85	49.1	15	39.5	0.28
Passive anal sex without condom†	74	42.8	19	50.0	0.42
Active fisting†	29	16.8	7	18.4	0.81
Passive fisting†	22	12.7	3	7.9	0.41
Had group sex*	80	46.2	18	47.4	0.90
Visited a sex club*	109	63.0	23	60.5	0.78
Visited a sex party*	36	20.8	12	31.6	0.15
Met sex partner through internet*	102	59.0	18	47.4	0.19
Had sex abroad*	105	60.7	19	50.0	0.23
(D) STI: history and diagnoses					
History of STI	51	29.5	7	18.4	0.17
HIV infected‡	59	34.3	21	58.3	0.007
Syphilis diagnosis	10	5.8	0	0	0.13
Gonorrhoea diagnosis	13	7.5	0	0	0.08
Chlamydia diagnosis	30	17.3	7	18.4	0.87
(E) Other possible risk factors					
Regularly attends the gym*	109	63.0	20	52.6	0.24
Regularly plays in a team sport*	13	7.5	0	0	0.08
Regularly visits the sauna*	110	63.6	23	60.5	0.72
Regularly takes a public shower*	103	59.5	25	65.8	0.48
Regularly travels abroad*	149	86.1	32	84.2	0.76
Regularly shaves					
Facial hair	165	95.4	38	100	0.18
Pubic hair	149	86.1	31	81.6	0.47
Body hair	110	63.6	20	52.6	0.21
Has pets	45	26.0	11	29.0	0.71
Works in healthcare	14	8.1	3	7.9	0.97
Was admitted to hospital*	9	5.2	4	10.5	0.22
Had surgery*	23	13.5	8	21.6	0.21

Continued

Table 2 Continued

	S aureus negative N=173		*S aureus* positive N=38		
	N	Per cent	N	Per cent	p Value
Had a blood transfusion*	6	3.5	1	2.6	0.79
Had enemas*	49	28.3	14	36.8	0.30
Frequently bites his fingernails	55	31.8	11	29.0	0.73
Has been circumcised	36	20.8	11	29.0	0.28

*During the previous year.
†In the past 6 months.
‡*HIV status missing for three patients who did not want to be tested.
GHB, γ-hydroxybutyric acid; MSM: men who have sex with men; *S aureus*, *Staphylococcus aureus*; STI, sexually transmitted infection; XTC, MDMA/methamphetamine.

S aureus colonisation. We attribute the more common colonisation among HIV-positive participants to their immunocompromised status. Unfortunately, we neither have data on virological, immunological or clinical parameters of HIV infection, nor about use of antiretroviral drugs. We did not observe an increased risk of *S aureus* nasal carriage among HIV infected, as was reported earlier.[28]

In contrast to Southern European countries, the Netherlands has a low rate of HA-MRSA, probably owing to the aforementioned search-and-destroy policy. The restricted use of β-lactam antibiotics outside of hospitals, in the community, might explain the low prevalence of CA-MRSA. Europe has not yet been confronted with CA-MRSA on a wide scale[23] contrary to Canada and the USA where high prevalences are found.[9 12 13 21–23] Yet, in contrast to low prevalences of HA-MRSA and CA-MRSA in the Netherlands, screening of Dutch workers with livestock has revealed that 39% of slaughterhouse pigs and >20% of pig farmers are asymptomatic carriers of LA-MRSA belonging to sequence-type (ST) 398.[14] The two MRSA strains isolated in our study were both unrelated to this LA-MRSA epidemic.

In conclusion, CA-MRSA among MSM visiting the STI outpatient clinic in Amsterdam is rare. Although genital *S aureus* colonisation was more common among HIV-infected MSM, we found no association between high-risk sexual behaviour and genital colonisation with *S aureus*. In the Netherlands there is no indication for MRSA screening of MSM attending STI clinics.

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Data sharing statement Technical appendix, statistical code and dataset available from the HJCdV at Dryad repository, who will provide a permanent, citable and open access home for the dataset. Extra data can be accessed via the Dryad data repository at http://datadryad.org/ with the doi:10.5061/dryad.569j0.

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