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Brief report

Prevalence and antimicrobial susceptibility profile of *Corynebacterium glucuronolyticum* in genitourinary tract samples

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ABSTRACT

Introduction: *Corynebacterium glucuronolyticum* (*C. glucuronolyticum*) is a species recently recognized as a potential pathogen of the male genitourinary tract. The objective is to determine the prevalence of *C. glucuronolyticum* in genitourinary tract samples as well as their antimicrobial susceptibility profile.

Methods: A prospective study was conducted from 1st of November 2021 to the 30th of November 2022, for all genitourinary tract samples collected from male patients with suspicion of balanitis, prostatitis and urethritis. Antimicrobial susceptibility testing was performed in all *C. glucuronolyticum* isolates.

Results: A total of 73 *C. glucuronolyticum* isolates from 693 clinical specimens were obtained. This represents an overall *C. glucuronolyticum* prevalence of 10.5%. All strains were susceptible to vancomycin, linezolid and rifampicin, whereas 94%, 68% and 65% were resistant to clindamycin, tetracycline and ciprofloxacin, respectively.

Conclusion: Clinical microbiology laboratories should perform antimicrobial susceptibility testing against *C. glucuronolyticum* due to the significant rate of resistance to ciprofloxacin and tetracycline.

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Prevalencia y perfil de sensibilidad antimicrobiana de *Corynebacterium glucuronolyticum* en muestras del tracto genitourinario

RESUMEN

Introducción: *Corynebacterium glucuronolyticum* (*C. glucuronolyticum*) es un microorganismo reconocido recientemente como patógeno del tracto genitourinario. El objetivo es determinar la prevalencia de *C. glucuronolyticum* en muestras del tracto genitourinario, así como su perfil de sensibilidad antimicrobiana.

Métodos: Se realizó un estudio prospectivo del 1 de noviembre del 2021 al 30 de noviembre del 2022 de todas las muestras recogidas de pacientes con sospecha de balanitis, prostatitis y uretritis. Se realizaron pruebas de sensibilidad a todos los aislados de *C. glucuronolyticum*.

Resultados: Se obtuvieron un total de 73 aislados de *C. glucuronolyticum* de 693 muestras. Esto representa una prevalencia del 10,5%. Todas las cepas fueron sensibles a vancomicina, linezolid y rifampicina, mientras que el 94, el 68 y el 65% fueron resistentes a clindamicina, tetraciclina y ciprofloxacino, respectivamente.

Conclusión: Los laboratorios de microbiología deberían realizar pruebas de sensibilidad a *C. glucuronolyticum* debido a la importante tasa de resistencia a ciprofloxacino y a la tetraciclina.

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Palabras clave:

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Introduction

Corynebacterium glucuronolyticum was isolated for the first time in 1995 by Funke et al. from male patients with genitourinary infections.¹ That same year, Riegel et al., described a new species named *Corynebacterium seminale*, mainly from semen specimens.² A comparative phylogenetic analysis, chromosomal DNA–DNA hybridization, and 16S rRNA gene sequencing data of these microorganisms, revealed these two species were indeed the same one.^{3,4}

C. glucuronolyticum is a Gram-positive, facultative-anaerobic carbohydrate fermenting, and non-lipophilic species yielding white–yellowish on sheep blood agar.

In recent years, *C. glucuronolyticum* has been considered a potential pathogen associated with infections such as urethritis, balanitis or prostatitis in males.^{5,6} It was also shown that this species may have influence on several semen parameters as well.⁷

However, there are few data about true frequency of occurrence of *C. glucuronolyticum* in routine clinical laboratories as well as its antimicrobial susceptibility. Therefore, the aim of this study is to determine the prevalence and the antimicrobial susceptibility profile of *C. glucuronolyticum*.

Methods

We conducted a prospective study of all genital samples collected from male patients with suspicion of balanitis, prostatitis and urethritis from 1st of November 2021 to the 30th of November 2022.

Urethral swabs and sub-preputial specimens were processed using microbiological standard culture procedures. Only semen specimens were culture quantitatively and those specimens that yielded *C. glucuronolyticum* with colony counts larger than 10⁴ CFU/mL were included for antimicrobial susceptibility testing.

Identification of the isolates was performed by MALDI-TOF® (Bruker Daltonics, Germany). If the initial run gave a score value of <2.0, the bacterial material was retested. MICs of the following 10 antimicrobial agents were determined using the E-test method (bioMérieux, Marcy l'Étoile, France): penicillin, ceftriaxone, meropenem, vancomycin, clindamycin, linezolid, ciprofloxacin, tetracycline, rifampicin and daptomycin. Selection of antimicrobial agents tested were based upon physician prescribed patterns and those with CLSI or EUCAST breakpoints. All susceptibility tests were performed on Mueller-Hinton with 5% defibrinated horse blood and 20 mg/L β-NAD (bioMérieux, Marcy l'Étoile, France). The culture plates were inoculated with a bacterial suspension adjusted to a turbidity equivalent to that of a 0.5 McFarland standard and incubated 5% CO₂ for 24 h. Isolates with insufficient growth after 24 h incubation, were incubated again, and inhibition zones read after 48 h.

MIC results were interpreted according to EUCAST breakpoints (2024), except for meropenem and ceftriaxone, which do not have breakpoints on EUCAST, and the Clinical and Laboratory Standards Institute (CLSI, M45 3rd ed.) interpretive criteria for *Corynebacterium* species were applied.

The presence of coinfections with other sexually transmitted pathogens (such as *Chlamydia trachomatis*, *Neisseria gonorrhoeae*, *Mycoplasma genitalium* and *Trichomonas vaginalis*), was detected by employing appropriate microbiological diagnostic procedures and PCR with Alinity mSTI Assay (Abbott).

Results

A total of 693 clinical specimens were collected from male patients with suspicion of balanitis, prostatitis and urethritis. The isolates were recovered from: urethral swabs (373), semen (146) and sub-preputial swabs (174).

During the study period, a total of 73 *C. glucuronolyticum* isolates were obtained. The distribution of *C. glucuronolyticum* in all clinical specimen sources were: urethral exudates 41 (56%), semen 22 (30%) and sub-preputial swabs 10 (14%). This represents an overall *C. glucuronolyticum* prevalence in our institution of 10.5%. Coinfections with other of the main urethritis pathogens were detected in 8 (12%) of the samples, but only from urethral swabs.

All isolates, except for two (97%), were identified with scores of ≥2. Those isolates whose identification had a score less than 2 were re-analyzed. In both strains a greater score than 2 was obtained after subculture.

Susceptibility testing was performed for all 73 isolates. The MIC range, MIC₅₀, and MIC₉₀ and the percentage of isolates susceptible to each antimicrobial agents tested are shown in Table 1.

All *C. glucuronolyticum* isolates were fully susceptible to vancomycin, linezolid and rifampicin. The highest percentage of resistance was found for clindamycin 94%, followed by tetracycline and ciprofloxacin with 68% and 65% respectively. Rates of resistance for ceftriaxone and meropenem were lower: 32% and 3% respectively. No resistance was found for penicillin although a significant number of ceftriaxone-resistant strains (12 of 73 strains, 23%) were intermediate (MIC 0.25 mg/L) according to CLSI breakpoints. Although no breakpoints are available for daptomycin, in either CLSI or EUCAST, potent activity against *C. glucuronolyticum* was observed, with MIC_{50/90} of ≤0.016/0.016 mg/L respectively.

We also compared the percentages of resistance of each antibiotic between the different sample types (Table 2). We found that MICs and the percentages of resistance did not change significantly, except for tetracycline, which was more resistant in urethral and sub-preputial swabs isolates (78% and 90%, respectively), than in semen (41%) ($p < 0.05$).

Table 1
Susceptibility of 73 *C. glucuronolyticum* clinical isolates against 10 antimicrobial agents.

Antimicrobial agent	Range (mg/L)	MIC (mg/L)		EUCAST			CLSI		
		MIC ₅₀	MIC ₉₀	%S	%I	%R	%S	%I	%R
Penicillin	0.03–0.25	0.12	0.25	0	100	0	76.4	23.6	0
Ceftriaxone	0.12–>32	1	32	–	–	–	65.3	2.8	31.9
Meropenem	0.03–1	0.12	0.5	–	–	–	84.7	12.5	2.6
Vancomycin	0.25–1	0.5	0.5	100	–	0	100	–	0
Daptomycin	<0.016–0.016	<0.016	<0.016	–	–	–	100	–	0
Ciprofloxacin	0.06–>32	8	>32	0	34.7	65.3	34.7	0	65.3
Clindamycin	0.12–>256	>256	>256	5.6	–	94.4	5.6	0	94.4
Linezolid	0.03–0.12	0.06	0.12	100	–	0	100	–	0
Tetracycline	0.03–32	8	>32	31.9	–	68.1	37.5	30.6	31.9
Rifampicin	0.002–0.003	0.002	0.003	100	–	0	100	0	0

Table 2

Percentages of resistance of each antimicrobial agent between different sample types.

Antimicrobial agent ^a	Urethral swabs (%)	Sub-preputial swabs (%)	Semen (%)	
Ceftriaxone	35	20	32	NS ^b
Meropenem	2.5	0	4.5	NS
Ciprofloxacin	70	50	73	NS
Clindamycin	95	100	91	NS
Tetracycline	78	90	41	<i>p</i> < 0.05

^a No resistance was found for: penicillin, vancomycin, daptomycin, linezolid and rifampicin.^b Not significant.

Discussion

Our study of *C. glucuronolyticum* strains recovered from a large prospective population-based cohort of patients with suspicion of balanitis, prostatitis and urethritis provides one the largest report of antimicrobial susceptibility test results. In addition, we provide data about the frequency of *C. glucuronolyticum* in male urogenital tract specimens. In our institution, this represents an overall prevalence of 10.5%. However, much lower frequencies had been found: 1% from clinically significant semen specimens, and 5% from urethral swabs.^{8,9} The frequency differences among reports may be due to the design of the studies or differences between the populations analyzed. In any case, these data show a relevant number of *C. glucuronolyticum* isolates and leads to considering this species as potential pathogen when it is isolated from male genital tract samples.

However, being able to differentiate between colonization and infection in *C. glucuronolyticum* may be difficult when it is isolated with other microorganisms that could be the etiological cause of the clinical picture. In our study, other pathogenic microorganisms were isolated in near to 12% of the patients. This result is similar to that found in other study, which found 12.5%.⁸ However, prospective clinical studies are needed in order to assess the clinical role of *C. glucuronolyticum* on this polymicrobial infections.

Regarding to antimicrobial susceptibility, as previously reported, all tested isolates were susceptible to vancomycin, rifampicin and linezolid.^{7,8,10,11} Acquired clindamycin resistance seems to be common in *C. glucuronolyticum* since only 6% of isolates were susceptible with MIC₅₀ and MIC₉₀ values >256 mg/L. This high percentage of resistance is consistent with other studies that also reported a high frequency of clindamycin resistance in clinical isolates of *C. glucuronolyticum* ranging from 60 to 93%.^{7,8,10,11}

We also documented high rates of resistance to tetracycline and ciprofloxacin (68% and 65% respectively). A similar susceptibility profile, although with lower percentages of resistance, has been reported.^{7,8,10,11} Tetracycline-resistant strains showed a bimodal MICs distribution, which suggests the existence of various resistance mechanisms. The use of tetracycline in the treatment of other genitourinary infections may be the cause of this high rate of resistance.

According to the MIC₅₀ and MIC₉₀ values of our isolates, ciprofloxacin demonstrated low activity against *C. glucuronolyticum*. The MIC distribution for ciprofloxacin showed a bimodal profile with a population of highly-resistant strains (MICs >2 mg/L). This means a high level of resistance to ciprofloxacin. In previous reports lower ciprofloxacin resistance has been documented ranging from 26.6% to 57%, but it seems that resistance to this antibiotic is increasing, and it have to keep in mind that could fail as treatment of this infections.

We further found resistance to ceftriaxone and meropenem, following CLSI breakpoints. The meropenem-nonsusceptible isolates were also reproducibly resistant to ceftriaxone (≥4 mg/L). However, a significant number of these strains (12 of 73 strains, 23%) that were found to be resistant to ceftriaxone have an elevated

penicillin MIC of 0.25 mg/L. These strains were classified as susceptible to penicillin according to EUCAST breakpoints, but in the intermediate category based on CLSI. From our data, we are unable to determine the reason for the increasing of penicillin MICs in ceftriaxone-nonsusceptible isolates.

Our study also shows the emergence of multidrug resistance to ciprofloxacin and tetracycline. About one-half of the isolates (48%) nonsusceptible to ciprofloxacin, were also resistant to tetracycline, indicating the limited oral therapeutic options and a risk of clinical failure by treating patients with these antimicrobial agents.

In conclusion, we provide data about the prevalence of *C. glucuronolyticum* in genitourinary tract samples and, show high rates of resistance to ciprofloxacin and tetracycline. Finally, our results highlight the need to routinely perform susceptibility testing on clinically significant *C. glucuronolyticum* isolates.

Conflict of interest

The authors declare that they have no conflict of interest.

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