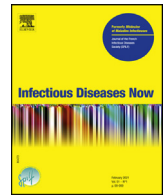




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Original article

Prevalence and risk factors for gonococcal infection in Reunion Island

A. Saïb^a, N. Bouscaren^b, B. Berçot^{c,d}, A. Duchateau^e, G. Miltgen^f, R. Rodet^g, G. Wartel^g,
F. Andry^a, S. Iacobelli^h, A. Bertolotti^{a,b,*}

^a CHU Réunion, service des maladies infectieuses – dermatologie, Saint-Pierre, Reunion

^b Inserm CIC1410, CHU Réunion, Saint-Pierre, Reunion

^c Département des agents infectieux, unité fonctionnelle de bactériologie, hôpital Saint-Louis, Assistance publique–Hôpitaux de Paris, Paris, France

^d Université Paris Diderot, UMR 1137, IAME, Sorbonne-Paris Cité, Paris, France

^e CHU Réunion, service de gynécologie, Saint-Pierre, Reunion

^f CHU Réunion, service de microbiologie, Saint-Denis, Reunion

^g CHU Réunion, service des maladies infectieuses, Saint-Denis, Reunion

^h CHU Réunion, service de néonatalogie, Saint-Pierre, Reunion

ARTICLE INFO

Article history:

Received 19 November 2021

Accepted 8 December 2021

Available online xxx

ABSTRACT

Objective: To determine the prevalence and risk factors for gonococcal infection, and the resistance profile of *Neisseria gonorrhoeae* (NG) in Reunion Island.

Patients and methods: All patients who visited the four sexually transmitted infection (STI) clinics of Reunion Island between January 2017 and December 2018 were screened by multiplex polymerase chain reaction. Data on patient characteristics were collected using a self-administered questionnaire (reason for screening, marital status, risk-taking behaviors, place of birth, employment status, type of health care coverage, sexual orientation, number of sexual partners, occurrence of extra-marital relationships, history of STIs, and symptomatology. Precarity was defined as being unemployed and/or receiving universal health insurance).

Results: The prevalence of NG ($n=4289$) in the screened population was 2.8% (95% CI [2.3–3.3]). Minors were especially at-risk (4.4% (95% CI [2.6–7])) and especially girls (5.6% (95% CI [3.2–8.9])). The prevalence observed in the homosexual population was 4.0% [2.6–5.9]. Gonococcal infection was asymptomatic in 56 (69%) patients. For all infection sites, the main risk factors were male minors ($P=0.019$), individuals living in conditions of precarity ($P=0.023$), individuals co-infected with chlamydia ($P<0.001$) or syphilis ($P<0.001$), and individuals of foreign origin ($P=0.006$). No NG strain was resistant to ceftriaxone. Strains were resistant to penicillin G, ciprofloxacin, and azithromycin in 22% (20/91), 38% (35/91), and 1% (1/91) of cases, respectively.

Conclusion: The prevalence of NG in patients visiting STI clinics in Reunion Island is particularly high among minors. Prevention programs targeting this population should be reinforced and screening should be facilitated in school settings.

1. Introduction

Gonorrhoea is a sexually transmitted infection (STI) caused by *Neisseria gonorrhoeae* (NG). The number of cases of gonococcal infection is on the rise in metropolitan France [1,2], a public health problem compounded by the development of NG resistance [3,4]. According to the World Health Organization, 86.9 million cases of gonorrhoea were reported worldwide in 2016, compared to 78 million in 2012 [5]. The incidence is highest in Africa and the Western

Pacific (China, Australia) [6,7], regions with which Reunion Island is now building ties.

Published data for metropolitan France indicate that men who have sex with men (MSM) account for 71% of cases of gonococcal infection and that the 20–29 age group is the most affected among heterosexuals [8]. However, few data are available on NG prevalence in Reunion Island [9]. Moreover, while at-risk populations have been identified at the European level and recommendations have been issued accordingly [10,11], no study has evaluated the risk factors for gonococcal infection in Reunion Island.

This is unfortunate, as this French overseas department is home to the youngest and most precarious population in France and presents with high rates of underage pregnancy and abortion [12]. The aim of our study was to determine the prevalence and risk factors for gonococcal infection and the antibiotic resistance profile of NG in Reunion Island.

* Corresponding author at: Service des maladies infectieuses – dermatologie, INSERM CIC 1410, CHU de la Réunion, Saint-Pierre, Reunion.
E-mail address: antoine.bertolotti@yahoo.fr (A. Bertolotti).

<https://doi.org/10.1016/j.idnow.2021.12.003>

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Table 1
Prevalence of *Neisseria gonorrhoeae* according to sex, age, and sexual orientation, overall and per infection site, $n = 118$, 2017–2018.

	All infection sites		Pharyngeal site		Urogenital site		Anal site	
	Prevalence % [95% CI]	P^a	Prevalence % [95% CI]	P^a	Prevalence % [95% CI]	P^a	Prevalence % [95% CI]	P^a
Total population	2.8% [2.3–3.3]	NA	1.6% [1.1–2.3]	NA	2.8% [2.3–3.5]	NA	2.3% [0–0]	NA
Sex		0.928		0.016		0.163		0.239
Men	2.8% [2.1–3.6]		2.6% [1.6–4.1]		2.4% [1.6–3.3]		1.8% [0.9–3.4]	
Women	2.7% [2.1–3.5]		1.1% [0.7–1.9]		3.2% [2.4–4.2]		2.9% [1.6–4.8]	
Age group		<0.001		0.859		<0.001		0.719
<18 years	4.4% [2.6–7]		1.5% [0.3–4.4]		5.8% [3.3–9.4]		2.6% [0.3–9.4]	
[18–25[3.7% [2.8–4.8]		2% [1.1–3.2]		4.2% [3.1–5.7]		2.9% [1.5–5]	
[25–30[2% [1.1–3.2]		1.4% [0.5–3.1]		1.9% [0.9–3.3]		1.7% [0.3–4.9]	
>30	1.7% [1.1–2.5]		1.5% [0.7–2.7]		1.2% [0.6–2]		1.8% [0.7–3.8]	
Sexual orientation		0.044		0.001		0.158		0.034
Heterosexual	2.6% [2.1–3.1]		1.2% [0.7–1.8]		3.1% [2.4–3.8]		1.7% [0.9–3]	
Homosexual	4% [2.6–5.9]		3.6% [1.9–6.2]		1.4% [0.5–3.1]		3.9% [2.0–6.8]	

Parameters showing statistical significance ($p < 0.05$) are highlighted in bold. CI: confidence interval; NA: not applicable.

^a Chi² test.

2. Patients and methods

This descriptive, cross-sectional study evaluated all patients who visited the four STI screening centers of Reunion Island (North, West, South infectiology, and South gynecology clinics) between January 2017 and December 2018.

All patients, symptomatic or not, who consented to participate in the study were anonymized and asked to respond to a standardized self-administered questionnaire. The following variables were collected: reason for screening, marital status, risk-taking behavior, place of birth, employment status, type of health care coverage, sexual orientation, number of sexual partners, occurrence of extra-marital relationship, history of STIs, and symptomatology. Precarity was defined as being unemployed and/or receiving universal health insurance (French equivalent of the US Medicaid program). Urogenital, pharyngeal, and anal samples were screened for NG, *Chlamydia trachomatis*, and *Mycoplasma genitalium* using multiplex polymerase chain reaction (PCR). Other STIs (syphilis, hepatitis B and C, and human immunodeficiency virus) were detected by serology. Antibigrams were performed on positive gonococcal cultures collected using gradient-strip (E-Test, bioMérieux, Marcy l'Étoile, France) according to EUCAST recommendations.

Qualitative variables were expressed as absolute numbers and percentages. Quantitative variables were expressed as means with standard deviation or with min/max values. Confidence intervals were set at 95% (95% CI). Risk factors were identified in multivariate analysis using a stepwise logistic regression. Variables included in the initial multivariate model were the risk factors identified in the literature and the potential confounding factors with a P -value < 0.2 in univariate analysis. All analyses were performed using STATA V13.1 software (StataCorp LP, Lakeway Drive, College Station, Texas 77845 USA).

This study was conducted according to reference methodology MR-004 of the French Data Protection Authority (French acronym CNIL). Informed consent was obtained from all participants and data were processed anonymously. The study was registered with the National Institute of Health Data under number MR 0808040220.

3. Results

Between January 2017 and December 2018, 4289 PCR tests for NG were performed in 9267 patients who visited the North, South infectiology and South gynecology STI clinics. Gonococcal infection was detected in 118 patients. The overall prevalence of NG in the screened population was 2.8% (95% CI [2.2–3.3]) for all

infection sites combined. There was no difference in prevalence between men and women for all age groups and all infection sites combined. The most common site of infection was the urogenital tract. The prevalence of NG was high among minors, particularly in the urogenital tract (5.8%) [3.3–9.4]. Female minors had a prevalence of 5.6% [3.2–8.9], while male minors had a prevalence of 1.0% [0.0–5.4].

In the homosexual population, which consisted exclusively of MSMs, a prevalence of 4.0% [2.6–5.9] was observed for all infection sites combined, with anal and pharyngeal infections being predominant (Table 1).

Among all patients with NG, 38 patients were co-infected with *C. trachomatis*, eight with syphilis, five with *C. trachomatis* + syphilis, four with *C. trachomatis* + *Mycoplasma genitalium*, three with *M. genitalium*, one with HIV + *M. genitalium*, and one with HIV. Past history of STI were reported by 32 patients, nine already had NG. No patient had viral hepatitis.

Gonococcal infection was asymptomatic in 56 (69%) patients, 29 of whom were male and 27 were female (clinical data were missing for 29 patients). In the South infectiology clinic, 25.6% of infected patients had burning on urination and 27.9% had purulent genital discharge. No cases of proctitis were described in patients with a positive anal sample.

In univariate analysis, for all infection sites combined, the following risk factors were statistically significant: age under 18 years, precarity, history of STI, and co-infection with *C. trachomatis*, *M. genitalium*, or *Treponema pallidum*.

In multivariate analysis, for all infection sites combined, an increased risk was found in male minors ($P = 0.019$), individuals living in conditions of precarity ($P = 0.023$), individuals co-infected with *C. trachomatis* ($P < 0.001$) or *T. pallidum* ($P < 0.001$), and individuals of foreign origin ($P = 0.006$) (Table 2).

Gonococcal infection in the anal canal was associated with concomitant pharyngeal or urogenital infection, with an incidence risk ratio of 6.6 ([1.9–22.9] $P = 0.003$) and 4.9 ([1.4–16.9] $P = 0.012$), respectively (Table 3).

A total of 91 NG strains collected from the 118 PCR-positive patients were isolated in cultures. All tested strains were susceptible to ceftriaxone. Strains were resistant to penicillin G, ciprofloxacin, and azithromycin in 22% (20/91), 38% (35/91), and 1% (1/91) of cases, respectively.

4. Discussion

The prevalence of NG in patients visiting STI clinics in Reunion Island is different from mainland France. In Reunion Island, for men, this prevalence is slightly lower (2.8%) than in mainland France

Table 2
Infections with *Neisseria gonorrhoeae*, all infection sites, univariate and multivariate analysis, n = 118, Reunion Island, 2017–2018.

	Univariate analysis			Multivariate analysis	
	n/N	IRR [95% CI]	p	IRR [95% CI]	p
Total population	118/4289				
Sex			0.928		0.019
Men	56/2006	ref		2.8 [1.2–6.4]	
Women	62/2258	1 [0.7–1.4]			
Age			0.047		0.014
< 18 years	18/409	2.6 [1.4–4.7]		3.0 [1.3–7.4]	
> 18 years	98/3834	ref			
Sexual orientation			0.115		
Heterosexual	94/3665	ref			
Homosexual	24/600	1.6 [1–2.5]			
History of STI			0.01		
Yes	32/702	1.8 [1.2–2.7]			
No/unknown	60/2354	ref			
Precarity ^a			0.002		0.023
No	52/2533	ref			
Yes	26/1741	1.8 [1.2–2.5]		2.4 [1.1–5]	
Region of birth			0.218		
Metropolitan France	25/1228	ref			
Reunion Island	52/2833	1.4 [0.9–2.3]		0.9 [0.4–2.1]	0.775
Foreign country	8/248	1.6 [0.7–3.5]		27.0 [2.6–274.4]	0.006
Condom misuse			0.565		
No	2/141	ref			
Yes	61/2401	2 [0.5–8]			
Unknown	49/1747	2 [0.5–8.1]			
Number of partners			0.123		
[0–1]	24/1030	ref			
[2–5]	51/1767	1.2 [0.8–2]			
[6–10]	7/341	0.9 [0.4–2]			
> 10	9/150	2.6 [1.2–5.5]			
Co-infections					
<i>Chlamydia trachomatis</i>	47/118	7.1 [4.9–10.2]	< 0.001	4.3 [2.1–8.8]	< 0.001
<i>Mycoplasma genitalium</i>	8/61	2.4 [1.2–5.1]	0.019	1.5 [0.5–4.4]	0.451
<i>Treponema pallidum</i>	13/105	5.1 [2.9–9.1]	< 0.001	5 [2.3–0.01]	< 0.001

Parameters showing statistical significance ($p < 0.05$) are highlighted in bold. IRR: incidence risk ratio; CI: confidence interval.

^a Defined as: unemployed or receiving social security benefits.

Table 3
Anal screening for *Neisseria gonorrhoeae*, n = 966, multivariate analysis, Reunion Island, 2017–2018.

Infection site	Multivariate analysis	
	IRR [95% CI]	p
Urogenital	4.9 [1.4–16.9]	0.012
Pharyngeal	6.6 [1.9–22.9]	0.003

Parameters showing statistical significance ($p < 0.05$) are highlighted in bold. IRR: incidence risk ratio; CI: confidence interval.

(3.8%), but for women it is more than twice higher (2.7% vs. 1.2%) [2]. While the prevalence of NG is increasing among ≥ 25 -year-olds in Europe [11], it is especially high among 18- to 25-year-olds (4.2% [3.1–5.7]) and minors (5.8% [3.3–9.4]) in Reunion Island. The prevalence of NG among women aged 15–24 years in STI clinics in South Africa was approximately 4.6%, while in Southern and Eastern Africa the prevalence was 1.7%. It was however much higher in high-risk populations in East Africa, such as sex workers (8.2%) [13]. In contrast, in Shenzhen, China, the prevalence of NG among 4812 women consulting to STI clinics was only 0.8% [14]. The prevalence of NG in people < 18 years old is not well reported in the literature and is often included in the 15–24 years old category [15]. In Reunion Island, we observe an equally high prevalence of other STIs (*C. trachomatis*, *M. genitalium*, syphilis) among these minors [16–19]. This discrepancy in results may be explained by condom misuse and lack of knowledge on STIs among Reunionese, a hypothesis reinforced by the high rates of underage pregnancy and abortion on the island.

Multivariate analyses indicated that age under 18 years, precarity, history of STI, and co-infection with *C. trachomatis*, *M. genitalium*, or *T. pallidum* are significantly associated with the risk of gonococcal infection [16]. They also showed an increased risk in male minors, individuals living in conditions of precarity, individuals co-infected with another STI, and individuals of foreign origin. Prevention programs targeting minors should therefore be reinforced and screening via self-swabbing should be facilitated in school settings. Moreover, given the high prevalence of NG observed in women under 25 years, routine conjunctival antibiotic prophylaxis in newborns may be needed to reduce the risk of neonatal gonococcal ophthalmia, as recommended in some countries [20].

The worldwide increase in gonococcal infections among MSM is also observed in Reunion Island, but the proportion of MSM affected by this infection compared to heterosexual men remains much lower than in mainland France (30% vs. 73%) [2,21]. In our study, oral carriage of NG was 3.6% [1.9–6.2] and anal carriage was 3.9% [2.0–6.8]. Moreover, 22.8% of patients had anal or pharyngeal infection without concomitant urogenital infection. At present, oral and anal NG screening is not routinely performed in Reunion Island, even though risk behaviors are reported by MSM patients [22]. Unfortunately, the lack of appropriate screening may lead to continued transmission of NG.

Seventy co-infections in 60 patients (37 females) were identified in patients with NG. *C. trachomatis*/NG co-infections are mostly described in female patients and are estimated between 7% and 40% in South Africa, Korea, or England [23–25]. Contrary to our population, co-infections with HIV in France were around 11% (1.9% in the present study) in 2016 and higher in MSM [8].

All strains tested were susceptible to ceftriaxone, i.e. the current reference treatment in metropolitan France. However, tested strains showed high resistance to fluoroquinolones (38% in the present study) – but at the lower end of the scale compared with mainland France (37.2% in 2017 and 59.8% in 2020, as per CNR data). Only one strain was resistant to azithromycin, and resistance to penicillin G was lower than resistance to ciprofloxacin. This latter finding is inconsistent with a recent study investigating the molecular epidemiology of NG in the Indian Ocean, which found penicillinase-producing strains of NG to be the most prevalent [26]. Of the three clusters identified by NG-MAST molecular typing in this study (the strains of which were mainly isolated in Reunion Island), the ST2318 cluster was composed of ciprofloxacin-resistant strains and showed ceftriaxone minimum inhibitory concentrations above the epidemiological cutoff (> 0.032 mg/L) [26]. This cluster also predominates in China, with which Reunion Island is now building ties and where an increase in NG resistance to third generation cephalosporins has been reported [27]. Global surveillance networks have highlighted that the resistance profile of NG varies according to geographical areas [28,29], confirming that migration has an impact on the origin and susceptibility of strains. Thorough surveillance of NG resistance with routine susceptibility testing should thus be continued in Reunion Island.

Our study has limitations:

- our findings only concern the population visiting STI clinics in Reunion Island, with one clinic failing to provide data due to difficulties in administering the questionnaire;
- our results cannot be compared with data from 2012 given the increased use of PCR tests for STI detection;
- prevalence in minors is likely underestimated because of poor availability of transport on the island [17];
- the lack of data on condom use and number of partners may have caused some results to be insignificant.

5. Conclusion

The overall prevalence of NG in patients visiting STI clinics in Reunion Island is close to that observed in other countries. However, age under 18 years, precarity, history of STI, and coinfection with another STI are significantly associated with the risk of gonococcal infection. As minors are especially at-risk, prevention programs targeting this population should be reinforced and screening via self-swabbing should be facilitated in school settings. Although all NG strains tested in our study were susceptible to ceftriaxone, thorough surveillance of NG resistance with routine susceptibility testing should be continued on the island.

Contribution of authors

A. B. conceptualized and designed the study.

A. B., A. S., N. B., A. D., R. R., G. W., and F. A. participated in the acquisition, analysis and interpretation of data.

A. S., N. B., and A. B. wrote the original article.

B. B., S. I., G. M., A. D., R. R., G. W., and F. A. critically reviewed the article.

All authors read and approved the final article.

Funding sources

None.

Disclosure of interest

The authors declare that they have no competing interest.

Ethical statement

This study was conducted according to reference methodology MR-004 of the French Data Protection Authority (French acronym CNIL). Informed consent was obtained from all participants and data were processed anonymously. The study was registered with the National Institute of Health Data under number MR 0808040220.

Acknowledgments

We would like to thank the board of medical informatics of Reunion Island hospitals, Aurélie Etienne, Luce Menudier, Yatrika Koumar, Cecile Saint-Pastou, Fanny Andry, Cecile Levin, Julien Jaubert, Naël Zemali, Nicolas Traversier, Marie-Christine Jaffar, Lucas Balloy, Stella Hoang, Carole Ricaud, Marie Lagrange-Xélot, Laurent Bellec, Barbara Kuli, Sandrine Gazaigues, Marie Pierre Moiton, Catherine Marimoutou, Marion Porcher, Emmanuelle Thore, Malik Boukerrou, Marc Gabriele, Catherine Gaud, as well as all members of the paramedical team of STI clinics and the CORE-VIH Océan Indien. We would like to thank Arianne Dorval, our copy editor.

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