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SHORT REPORT

Retrospective Analysis of Drug Sensitivity of *Neisseria gonorrhoeae* in Teaching Hospitals of South China

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Abstract: The aim of this study was retrospective analysis of drug sensitivity of *Neisseria gonorrhoeae* in two teaching hospitals of South China. A total of 304 *Neisseria gonorrhoeae* isolates obtained from patients in South China from 2016 to 2020 were evaluated. The MICs of penicillin, cefuroxime, ceftriaxone (CRO), cefepime, ciprofloxacin, ceftazidime and azithromycin (AZM) against the isolates were determined by the agar dilution method. Then, *Neisseria gonorrhoeae* isolates were categorized into sensitive, moderately sensitive and resistant according to MICs. Also, β-lactamases were detected by enzyme linked immunosorbent assay (ELISA). *Ureaplasma urealyticum* and *Mycoplasma hominis* were determined by culture in liquid medium, and *Chlamydia* was detected by rapid antigen test. The result showed there was 50.99%, 20.72%, 9.87%, 14.47%, 86.84%, 7.57%, 6.91%, 11.18% resistance to penicillin, cefuroxime, ceftriaxone, cefepime, ciprofloxacin, ceftazidime and azithromycin, respectively. Also, β-lactamase positivity was 53.29% and *Chlamydia* antigen positivity was 20.07%. *Ureaplasma urealyticum* and *Mycoplasma hominis* positivity was 11.84% and 6.25%, respectively. From 2016 to 2020, the resistant rate of ceftriaxone and azithromycin gradually increased. In conclusion, Southern China is among the area reporting gonococci with high-level resistance to AZM and CRO, so *N. gonorrhoeae* culture and drug sensitivity test will be vital for monitoring trends in antimicrobial resistance.

Keywords: drug sensitivity, *Neisseria gonorrhoeae*, retrospective analysis

Introduction

Neisseria gonorrhoeae infection, one of the most common sexually transmitted disease, is a global problem.[1] In mainland china, the incidence of *N. gonorrhoeae* infection has increased continuously, with the incidence rate among the top five of national notifiable infectious diseases.[2] A wide spectrum of clinical manifestations and complications of *N. gonorrhoeae* infection has been observed, and the vaccine against *N. gonorrhoeae* is not available at present. Therefore, the infection control predominantly relies on timely diagnosis and appropriate antibiotic therapy.[1–4] Over time, *Neisseria gonorrhoeae* has developed resistance to a broad range of antimicrobial agents. Some sensitive antibiotics, such as ceftriaxone, have been reported to have become ineffective in the recent years.[5,6] The rapid development of *N. gonorrhoeae* resistance to antimicrobial agents worldwide will threaten the management of *N. gonorrhoeae* infection.[1]

This study is a retrospective analysis of drug sensitivity of *Neisseria gonorrhoeae* in the two teaching hospitals of South China from 2016 to 2020.

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Materials and Methods

Retrospective analysis of drug sensitivity of *Neisseria gonorrhoeae* in two teaching hospitals of Guangzhou, South China from 2016 to 2020 was performed.

The demographic and clinical information of patients such as gender, age, and symptoms was collected using electronic case system. Each isolate was cultured and verified.[7] MIC for penicillin, cefuroxime, ceftriaxone (CRO), cefepime, ciprofloxacin, ceftazidime and azithromycin (AZM) were determined by the agar dilution method. Antimicrobial susceptibility was interpreted according to criteria defined by WHO.[8,9]

The β-lactamase was detected by enzyme linked immunosorbent assay (ELISA).[10] *Ureaplasma urealyticum* and *Mycoplasma hominis* was determined by culture in liquid medium, and *Chlamydia* was detected by rapid antigen test.[10] All the results were collected using electronic case system and clinical examination electronic system.

Statistical significance was assessed using SPSS 18.0. Chi-square tests were used for statistical analyses. A $P < 0.05$ was considered to be significant.

Results

Three hundred and four patients with *Neisseria gonorrhoeae* infection were included in this study. The study included 282 male and 22 females. The age range was from 16 to 75 years, with the average age 30.30±9.11 years. From 2016 to 2020, resistance rate to ceftriaxone was 6.38%, 8.06%, 8.86%, 14.29% and 11.67%, respectively, the average resistance was 9.87%. Resistance to azithromycin was 6.38%, 9.68%, 10.13%, 12.50% and 16.67%, respectively, in 2016 to 2020, and the average resistance was 11.18% (Table 1). The differences in the resistance rate between 2016 and 2020 were statistically significant for ceftriaxone and azithromycin ($P < 0.05$).

From 2016 to 2020, β-lactamase positive of *Neisseria gonorrhoeae* was rising every year ($P < 0.05$). *Neisseria gonorrhoeae* infection combined with Chlamydia infection and *Ureaplasma urealyticum* infection was also increased gradually ($P < 0.05$) (Table 2).

Table 1 Antimicrobial Resistance to *Neisseria gonorrhoeae* Infection from 2016 to 2020

Year	Gender	Age	Antimicrobial Resistance (%)						
			Penicillin	Cefuroxime	Cefepime	Ciprofloxacin	Ceftazidime	Spectinomycin	Ceftriaxone	Azithromycin
2016	M41, F6	29.82±7.00	44.68	14.89	19.15	87.23	12.77	8.51	6.38	6.38
2017	M59, F3	28.88±7.46	61.29	12.90	16.13	93.55	10.84	8.06	8.06	9.68
2018	M76, F3	29.41±8.41	37.97	15.40	15.63	75.95	13.63	5.06	8.86	10.13
2019	M59, F3	30.39±10.88	46.43	17.85	19.64	91.07	10.71	8.71	14.29	12.50
2020	M56, F4	34±11.05	66.67	10.00	16.67	90.00	13.67	6.67	11.67	16.67

Abbreviations: M, male; F, female.

Discussion

The vaccine against *N.gonorrhoeae* is not available at present; a wide spectrum of clinical manifestations and complications of *N. gonorrhoeae* infection have increased gradually. Therefore, *N.gonorrhoeae* infection control

predominantly relies on accurate diagnostics and timely antibiotic therapy following antibiotic sensitivity testing.[1–4]

In the recent years, the management of *N.gonorrhoeae* infection has been difficult because of the rapid development of resistance to a broad range of antimicrobial agents.[1]

In order to limit the development of antimicrobial resistance and ensure effective treatment, the therapy with ceftriaxone 250 or 500 mg administered intramuscularly plus azithromycin 1 or 2 g orally has been widely accepted as the first choice for the treatment of *N. gonorrhoeae* infection.[11] As the emergence of treatment failure with cephalosporins have been documented in several countries in the 2000s and the warning susceptibility of *N. gonorrhoeae*, some scholars recommend the use of 1000 mg ceftriaxone intramuscularly.[3] In this retrospective study, *N. gonorrhoeae* resistance rate to ceftriaxone was 6.38%, 8.06%, 8.86%, 14.29% and 11.67%, respectively, from 2016 to 2020. The average resistance was 9.87%. This is consistent with previous studies.[5–7]

Situated in Southern China, Guangzhou is the important node city of "the Silk Road" and "The Belt and Road", which has a large transient population of foreign visitors and business partners. The import and dissemination of antimicrobial resistance is a constant public health threat in Guangzhou. Ceftriaxone-resistant multidrug-resistant *N. gonorrhoeae* undermines the effectiveness of currently recommended first-line dual therapy. It is imperative to enhanced surveillance of antimicrobial susceptibility, in order to detect and monitor the resistance trends of *Neisseria gonorrhoeae*, so as to ensure the effectiveness of its treatment.[1,3]

In this study, resistance rate from 2016 to 2020 has increased significantly with regard to ceftriaxone and azithromycin. Also, *Neisseria gonorrhoeae* infection combined with *Chlamydia* infection and *Ureaplasma urealyticum* infection has also increased gradually. Pathogenic examination, especially *N. gonorrhoeae* culture and drug sensitivity test, is more important for the selection of sensitive antibiotics. A limitation of this study is that a small number of cases were assessed.

Ethics Statement

The study was approved by the Ethics Committee of the First Affiliated Hospital of Jinan University and the Third Affiliated Hospital of Southern Medical University. All subjects were adults and provided written informed consent.

Table 2 *Neisseria gonorrhoeae* Infection in Teaching Hospitals from 2016 to 2020

Year	Gender	Age	β-lactamase Positive	*Chlamydia* Antigen Positive	*Ureaplasma urealyticum* Positive	*Mycoplasma hominis* Positive	GC+ *Chlamydia*+ *UU* Positive	GC+ *Chlamydia*+ *Mh* Positive	GC+ *Chlamydia*+ *UU*+ *Mh* Positive
2016	M41, F6	29.82±7.00	42.55%	13.40%	7.02%	6.38%	8.33%	1.67%	1.67%
2017	M59, F3	28.88±7.46	40.32%	12.90%	9.68%	6.45%	8.93%	3.57%	1.79%
2018	M76, F3	29.41±8.41	48.10%	16.46%	10.13%	6.33%	7.60%	2.53%	2.53%
2019	M59, F3	30.39±10.88	67.86%	21.42%	14.29%	7.36%	8.06%	4.84%	3.22%
2020	M56, F4	34±11.05	68.33%	28.33%	17.00%	6.67%	12.77%	4.26%	4.26%

Abbreviations: M, male; F, female; *GC*, *Neisseria gonorrhoeae*; *UU*, *Ureaplasma urealyticum*; *Mh*, *Mycoplasma hominis*.

This study was conducted in accordance with the Declaration of Helsinki.

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Author Contributions

All authors made substantial contributions to conception and design, acquisition of data, or analysis and interpretation of data; took part in drafting the article or revising it critically for important intellectual content; agreed to submit to the current journal; gave final approval of the version to be published; and agree to be accountable for all aspects of the work.

Disclosure

The authors have no conflicts of interest to declare.

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