



# Evaluation of *Neisseria gonorrhoeae* Culture Results and Antibiotic Usage in Patients Presenting with Urethral Discharge: Four-Year Retrospective Study

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## Abstract

**Introduction:** The aim of this study was to evaluate the microbiological diagnostic results of *Neisseria gonorrhoeae* (*N. gonorrhoeae*) infections, assess the frequency of empirical antibiotic usage, and determine compliance with current treatment guidelines among patients presenting with urethral discharge.

**Methods:** A retrospective analysis was conducted among 387 patients admitted with suspected gonococcal infection between June 2014 and February 2018 to the Departments of Infectious Diseases, Urology, and Gynecology at Ankara Numune Training and Research Hospital. Demographic characteristics, microscopy and culture results, treatment protocols, and antibiotic prescriptions were obtained from hospital information systems. The chi-square test was applied for statistical analysis, and  $p < 0.05$  was considered statistically significant.

**Results:** A total of 387 patients with a mean age of  $32.6 \pm 10.8$  years were included; 99.9% ( $n=386$ ) were male and 0.1% ( $n=1$ ) were female. Among these patients, 73.9% ( $n=286$ ) were referred from the Urology outpatient clinic, whereas 26.1% ( $n=101$ ) were from Infectious Diseases. The overall isolation rate of *N. gonorrhoeae* was 13.7% ( $n=53$ ). Among patients who received empirical antibiotic therapy ( $n=79$ ), gonococcal culture positivity was 11.4% ( $n=9$ ), whereas positivity was 14.3% ( $n=44$ ) among those who did not receive empirical treatment ( $n=308$ ) ( $p > 0.05$ ). Antibiotics were prescribed based on culture results to 88.1% ( $n=341$ ) of patients. The most frequently prescribed antibiotic regimen was a combination of cephalosporin+doxycycline+azithromycin (19.1%). Among the 53 patients with gonococcal growth, antibiotics were prescribed to 96.2% ( $n=51$ ), yet the recommended standard regimen of cephalosporin+azithromycin was administered to only 7.5% ( $n=4$ ).

**Discussion and Conclusion:** This study revealed that culture and antimicrobial susceptibility testing were inadequately utilized in the diagnosis and management of gonococcal infections, and empirical antibiotic therapy demonstrated poor compliance with current guidelines. Increased clinical awareness and strict adherence to updated guidelines are required for the accurate diagnosis and effective treatment of gonococcal infections.

**Keywords:** Antibiotic therapy; antimicrobial resistance; *Neisseria gonorrhoeae*; urethritis.

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*Neisseria gonorrhoeae* (*N. gonorrhoeae*) infection is a sexually transmitted infection that is increasingly prevalent worldwide and causes significant morbidity [1–3]. Infection of mucosal surfaces such as the urethra, endocervix, rectum, oropharynx, and conjunctiva with *N. gonorrhoeae* results in urethritis, cervicitis, and pelvic inflammatory disease [4,5]. Each year, approximately 82 million new cases of gonorrhea are reported worldwide according to the World Health Organization (WHO) [3,5,6].

Recently, the increasing antibiotic resistance has created significant challenges in the control and treatment of gonorrhoeae infection [7,8]. Treatment options are currently quite limited due to the rapid development of resistance to penicillin, tetracyclines, and fluoroquinolones [9]. Due to the widespread use of cephalosporins, decreased susceptibility of gonococci to third-generation cephalosporins such as ceftriaxone and cefixime is considered a major threat to global health [9,10]. This situation highlights the importance of reviewing current treatment protocols and performing antimicrobial susceptibility testing regularly [6,10].

Studies on the frequency of gonococcal infection in Türkiye have reported significantly high prevalences, particularly in at-risk groups [11–13]. In a study conducted by Pelit and colleagues, *N. gonorrhoeae* was detected in 4.5% of men with urethritis symptoms [10], while in a study conducted by Aksu among sex workers, this rate was reported as 12.4% [12]. Other studies conducted across Türkiye also show that gonococcal infections are not adequately controlled due to barriers in accessing diagnosis and treatment and the lack of awareness [11–14].

The aim of this study was to evaluate patients presenting with complaints of urethral discharge in terms of *N. gonorrhoeae*, to emphasize the importance of culture and antibiogram instead of treating patients based only on symptoms, and to assess the compliance of drugs used in standard treatment with the recommendations of current guidelines.

## Materials and Methods

### Study Design and Patient Population

In this retrospective study, a total of 387 patients who applied to the Infectious Diseases, Urology, and Gynecology and Obstetrics outpatient clinics of Ankara Numune Training and Research Hospital with complaints of urethral discharge between June 2014 and February

2018 and who underwent urethral discharge microscopy and culture with a preliminary diagnosis of gonococcal infection were evaluated. The clinical and laboratory data of 387 patients were evaluated retrospectively using the hospital information management system (FONET) and the Medulla doctor system.

Data on the demographic characteristics of the patients (age and gender), the number of tests requested from clinical departments, microscopic examination and culture results, recommended treatment protocols, and post-treatment follow-up of the patients were collected. For microbiological examination of urethral discharge samples, smears were stained with Gram stain and cultured in Modified Thayer-Martin medium. The media were incubated for 24–48 hours at 35–37°C in an environment of 5% CO<sub>2</sub>. Standard biochemical methods were used for the identification of bacteria grown in culture. Antibiotic susceptibility testing of patients with positive culture results was performed by the disk diffusion method as recommended by the Clinical Laboratory Standards Institute (CLSI).

### Ethical Approval

The study was approved by the Ethics Committee of Ankara Numune Training and Research Hospital (dated 08/05/2018, decision no: E-18-1971 and 1971). Since the study was retrospective, informed consent was not obtained by its nature. The study was conducted in accordance with the Declaration of Helsinki.

### Statistical Analysis

Statistical analyses were conducted using IBM SPSS Statistics version 18.0. For continuous variables, the mean±standard deviation, minimum, and maximum values were calculated. Categorical variables were presented as counts and percentages. Differences between groups were evaluated using the chi-square test, and  $p<0.05$  was considered statistically significant.

## Results

In total, 387 patients were included in the study. The mean age of the patients was  $32.6\pm10.8$  years, and 99.9% ( $n=386$ ) of the patients were male. Among the 387 patients, 73.9% ( $n=286$ ) were admitted to Urology, and 26.1% ( $n=101$ ) were admitted to Infectious Diseases outpatient clinics. It is noteworthy that the number of tests requested from Urology clinics increased over the years. The distribution of 368 patients by year and clinic is shown in Table 1.

**Table 1.** Number of patients who requested urethral discharge microscopy by clinic and year

| Years                          | Department of Infectious Diseases<br>101 (26.1)<br>n (%) | Urology Department<br>286 (73.9)<br>n (%) |
|--------------------------------|----------------------------------------------------------|-------------------------------------------|
| 2014 (n=48)                    | 21 (43.8)                                                | 27 (56.3)                                 |
| 2015 (n=79)                    | 16 (20.3)                                                | 63 (79.7)                                 |
| 2016 (n=100)                   | 23 (25)                                                  | 69 (75)                                   |
| 2017 (n=144)                   | 37 (25.7)                                                | 107 (74.3)                                |
| 2018 (January-February) (n=24) | 4 (16.7)                                                 | 20 (83.3)                                 |

**Table 2.** Distribution of urethral discharge culture results in patients receiving and not receiving empirical treatment

|                                 | Percentage receiving empirical treatment (%)<br>79 (20.4) | Not receiving empirical treatment (%)<br>308 (79.6) |
|---------------------------------|-----------------------------------------------------------|-----------------------------------------------------|
| <i>N. gonorrhoeae</i> has grown | 9 (11.4)                                                  | 44 (14.3)                                           |
| Other microorganisms            | 49 (62.0)                                                 | 183 (59.4)                                          |
| No growth in culture            | 21 (26.6)                                                 | 81 (26.3)                                           |

**Table 3.** Post-culture antibiotic administration status and distribution of administered antibiotics

| Antibiotic                             | n   | %    |
|----------------------------------------|-----|------|
| Not given                              | 46  | 11.9 |
| Given                                  | 341 | 88.1 |
| Doxycycline                            | 20  | 5.4  |
| Cephalosporin                          | 13  | 3.4  |
| Quinolone+Doxycycline                  | 61  | 15.8 |
| Cephalosporin+Doxycycline              | 60  | 15.5 |
| Cephalosporin+Azithromycin             | 36  | 9.3  |
| Cephalosporin+Doxycycline+Azithromycin | 74  | 19.1 |
| Azithromycin+Doxycycline               | 28  | 7.2  |
| Other                                  | 28  | 7.2  |

**Table 4.** Distribution of antibiotics given to patients with positive gonococcal cultures

| Antibiotic                 | n  | %    |
|----------------------------|----|------|
| Not given                  | 2  | 3.8  |
| Given                      | 51 | 96.2 |
| Quinolone                  | 1  | 1.9  |
| Doxycycline                | 3  | 5.7  |
| Cephalosporin              | 5  | 9.4  |
| Quinolone+Doxycycline      | 6  | 11.3 |
| Cephalosporin+Doxycycline  | 10 | 18.9 |
| Cephalosporin+Azithromycin | 4  | 7.5  |
| Cephalosporin+Doxycycline  | 1  | 1.9  |
| Azithromycin+Doxycycline   | 14 | 26.4 |
| Other                      | 7  | 13.2 |

Of the 387 patients included in the study, 79 (20.4%) received empirical treatment, while 308 (79.6%) did not receive treatment. *N. gonorrhoeae* was grown in culture in 9 of 79 patients (11.4%) who received empirical treatment and in 44 of 308 patients (14.3%) who did not receive treatment, as shown in Table 2. No statistically significant difference was found between the two groups in terms of gonococcal growth rates ( $p>0.05$ ). Antibiotic treatment was recommended to a total of 341 (88.1%) patients based on culture results. The most frequently prescribed antibiotic combination, with a rate of 19.1% ( $n=130$ ), was cephalosporin+doxycycline+azithromycin. Other frequently recommended antibiotic combinations were quinolone+doxycycline 15.8% ( $n=61$ ) and cephalosporin+doxycycline 15.5% ( $n=60$ ). Table 3 shows the distribution of antibiotics prescribed according to culture results.

Fifty-one of the 53 patients whose cultures yielded *N. gonorrhoeae* were given antibiotic treatment. The most frequently prescribed treatment for these patients was the azithromycin+doxycycline combination (26.4%,  $n=14$ ), followed by cephalosporin+doxycycline (18.9%,  $n=10$ ). Only 4 patients (7.5%) were prescribed cephalosporin+azithromycin treatment, which is recommended as the standard regimen by the guidelines. Table 4 shows the distribution of antibiotic treatments given to patients with positive *N. gonorrhoeae* cultures.

## Discussion

In our study, a total of 387 patients presenting with urethral discharge complaints were evaluated, and the vast majority of the cases (99.9%) consisted of male patients. This finding is consistent with data in the literature indicating that men generally constitute the vast majority of symptomatic gonorrhea cases. According to WHO data, approximately 82 million new cases of gonorrhea are reported worldwide each year, and men tend to seek medical attention more frequently because they are often symptomatic<sup>[1]</sup>.

In our study, the rate of *N. gonorrhoeae* growth in culture was found to be 13.7%. This rate is higher than the 4.5% reported by Pelit et al.<sup>[13]</sup> in Türkiye but similar to the 12.4% reported by Aksu among sex workers<sup>[11]</sup>. Similar high prevalences have been reported in other studies conducted in our country<sup>[12,14]</sup>.

Although the rate of gonococcal growth in culture (11.4%) in patients given empirical treatment was lower than in those who did not receive empirical treatment (14.3%), it was not found to be statistically significant. This supports

the idea that empirical treatment has limited effectiveness in *N. gonorrhoeae* eradication and that treatment should be planned according to culture and antibiogram results. The literature also notes that high resistance rates increasingly limit empirical treatment approaches [8,10,15,16].

In our study, it was observed that the majority of the prescribed antibiotics (88.1%) were given according to culture results. The most frequently used antibiotic combination in these patients was cephalosporin+doxycycline+azithromycin (19.1%). However, the combination of cephalosporin+azithromycin, recommended as the standard treatment in the guidelines, was preferred by only 7.5%. This rate is parallel to other studies published in Türkiye, showing that full compliance with treatment protocols is generally low [17,18].

Today, the antibiotic resistance of *N. gonorrhoeae* has become a significant global health issue. According to Quillin and Seifert's research, treatment options have become very limited as bacteria become increasingly resistant to antibiotics such as penicillin, tetracycline, and fluoroquinolones [9]. In addition, the decreased susceptibility of gonococci to third-generation cephalosporins such as ceftriaxone and cefixime following widespread use of these drugs is considered a serious health threat [7,9].

Studies investigating the epidemiology of gonorrhea infections in Türkiye show that the prevalence of *N. gonorrhoeae* infections is high, especially in at-risk populations [11,19]. However, studies conducted in the general population indicate that awareness of gonorrhea infections is low among large segments of society and that access to healthcare services is insufficient [18,20].

It is noteworthy that there was only one female patient in our study. Gonococcal infections in women are often asymptomatic, leading to limited access to diagnosis and treatment, which causes the infection to spread silently and increases complications [21]. In this context, it is important to promote more active screening and diagnostic methods among female patients.

One of the significant limitations of our study is the risk of incomplete records and the inability to fully verify information due to the retrospective design. Additionally, methodological differences may limit the use of the disk diffusion method for conducting antibiotic susceptibility tests. The literature emphasizes that ensuring standardization in antibiotic susceptibility tests is critically important for the accurate evaluation of resistance rates [10,22].

## Limitations of the Study

The main limitations of this study are its retrospective design and the fact that the data were obtained retrospectively from hospital information management systems. Additionally, antimicrobial susceptibility testing was not routinely and systematically performed in patients with positive gonococcal culture results. This means that the data obtained do not fully reflect the antimicrobial resistance profile and limits our ability to evaluate antibiotic susceptibility. Although the sample size of the study was sufficient, the extremely low number of female patients made it impossible to conduct a clinical and epidemiological evaluation of gonorrhea infections in women. Therefore, the generalizability of our findings to the female population is extremely limited.

## Conclusion

In this retrospective study, it was determined that microscopy and culture methods were used at a low rate in the diagnosis of gonococcal infection in patients presenting with urethral discharge complaints and that empirical antibiotic treatment practices were widespread but insufficient in terms of adherence to guidelines. It was noteworthy that compliance with standard treatment protocols when prescribing antibiotics was low and that, despite culture results, appropriate treatment regimens were rarely applied. This indicates that the guidelines for gonorrhea treatment are not adequately reflected in clinical practice and that clinicians need to improve their adherence to current treatment protocols.

Our study highlights the need to increase clinical awareness for the effective treatment of gonococcal infections through rapid diagnosis, culture, and antibiotic susceptibility testing. Additionally, the very low number of female patients presenting with urethral discharge complaints indicates that diagnostic and screening programs for women need to be strengthened. In today's world, where antimicrobial resistance rates are rising globally, routinely conducting antibiotic susceptibility tests for *N. gonorrhoeae* and adopting a targeted treatment approach instead of empirical treatment is of critical importance. Finally, multidisciplinary approaches and continuous education for healthcare workers are of great importance in the fight against gonococcal infections.

**Ethics Committee Approval:** The study was approved by the Ethics Committee of Ankara Numune Training and Research Hospital (No: E-18-1971 and 1971, Date: 08/05/2018).

**Conflict of Interest:** The authors declare that there is no conflict of interest.

**Informed Consent:** Since the study was retrospective, informed consent was not obtained by its nature.

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