

CHARACTERISTICS AND MANAGEMENT OF GONORRHEA : A TEN YEARS SYSTEMATIC REVIEW

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ABSTRACT

Background: *Neisseria gonorrhoeae*, an obligate human pathogen, is a sexually transmitted disease that causes consequential worldwide morbidity both in resource-abundant and resource-limited nations, and its diagnosis and treatment require costly expenditures annually. Like other sexually transmitted infections (STIs), gonorrhea disproportionately impacts young adult populations.

The aim: *The aim of this study to show about characteristics and management of gonorrhea.*

Methods: *By the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) 2020, this study was able to show that it met all of the requirements. This search approach, publications that came out between 2014 and 2024 were taken into account. Several different online reference sources, like Pubmed, SagePub, and Google Scholar were used to do this. It was decided not to take into account review pieces, works that had already been published, or works that were only half done.*

Result: *In the PubMed database, the results of our search get 51 articles, whereas the results of our search on SagePub get 551 articles, on Google Scholar 2410 articles. Records remove before screening are 1219, so we get 1793 articles for screening. After we screened based on record exclude, we compiled a total of 12 papers. We included five research that met the criteria.*

Conclusion: *The management of N. gonorrhoeae infections was compromised by a low rate of examining sexual partners, females and testing extragenital specimens, screening for HIV, compliance to follow-up visits, access to nucleic acid amplification tests, and receiving questionable or even obsolete antimicrobial treatment. Therefore, more accurate and comprehensive management of gonorrhea is urgently needed.*

Keyword: *Gonorrhea, characteristic, management, treatment, Neisseria gonorrhoeae.*

INTRODUCTION

Neisseria gonorrhoeae is the second most common bacterial cause of sexually transmitted infections (STIs) in North America, following *Chlamydia trachomatis*. Globally, gonococcal infections are now an urgent problem because *N. gonorrhoeae* is capable of rapidly developing resistance to multiple antibiotic classes. Over time, *N. gonorrhoeae* has become less susceptible to numerous antibiotics, including the sulfonamides, penicillins, tetracyclines and fluoroquinolones. More recently, cases of resistance to cephalosporins, the current first-line treatment, have been reported.^{1,2}

Sexually transmitted infections (STIs) caused by the bacteria *Neisseria gonorrhoeae* (gonococcal infections) have increased 63% since 2014 and are a cause of sequelae including pelvic inflammatory disease, ectopic pregnancy, and infertility and can facilitate transmission of human immunodeficiency virus (HIV). Effective treatment can prevent complications and transmission, but *N. gonorrhoeae*'s ability to acquire antimicrobial resistance influences treatment recommendations and complicates control. In 2010, CDC recommended a single 250 mg intramuscular (IM) dose of ceftriaxone and a single 1 g oral dose of azithromycin for treatment of uncomplicated gonococcal infections of the cervix, urethra, and rectum as a strategy for preventing ceftriaxone resistance and treating possible coinfection with *Chlamydia trachomatis*. Increasing concern for antimicrobial stewardship and the potential impact of dual therapy on commensal organisms and concurrent pathogens, in conjunction with the continued low incidence of ceftriaxone resistance and the increased incidence of azithromycin resistance, has led to reevaluation of this recommendation.^{3,4}

Transmission of the bacteria has been reportedly found to take place during coitus through direct contact with mucous membranes in the oropharynx, anal canal, urogenital tract, and eyes (conjunctivitis). This often results in cervicitis in females and urethritis in males. Most males who suffer from symptomatic gonococcal urethritis, post-medical treatment, are no longer found to be contagious. However, the presence of untreatable gonorrhoea may increase the incidence of complications due to the infection. With over 78 million annual cases worldwide and limited treatment options in low-income nations and marginalised groups in wealthier countries.^{5,6}

Although *Neisseria gonorrhoeae* may also colonise the anal mucosa, nasopharyngeal, and ocular areas, its primary colonisation site is found to be the vaginal mucosa. The adverse outcomes mainly arise from the damage caused by the activation of the innate immune response at the colonisation sites since *N. gonorrhoeae* is not known to produce any potent exotoxins. In females, untreated infections of the ascending genital tract may lead to complications such as ectopic pregnancy, pelvic inflammatory illness, and infertility. Transmitting these bacteria from mothers to their unborn offspring may result in neonatal blindness. Untreated *N. gonorrhoeae* may lead to disseminated gonococcal infection, which is known to cause infectious arthritis and endocarditis. In some cases, *N. gonorrhoeae* may penetrate the circulation and disseminate, leading to cutaneous and tendon or joint infections and, rarely, endocarditis or meningitis.⁵

METHODS

Protocol

By following the rules provided by Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) 2020, the author of this study made certain that it was up to par with the requirements. This is done to ensure that the conclusions drawn from the inquiry are accurate.

Criteria for Eligibility

For the purpose of this literature review, we compare and contrast characteristics and management of gonorrhea. It is possible to accomplish this by researching or investigating characteristics and management of gonorrhea. As the primary purpose of this piece of writing, demonstrating the relevance of the difficulties that have been identified will take place throughout its entirety.

In order for researchers to take part in the study, it was necessary for them to fulfil the following requirements: 1) The paper needs to be written in English, and it needs to determine about characteristics and management of gonorrhea. In order for the manuscript to be considered for publication, it needs to meet both of these requirements. 2) The studied papers include several that were published after 2014, but before the time period that this systematic review deems to be relevant. Examples of studies that are not permitted include editorials, submissions that do not have a DOI, review articles that have already been published, and entries that are essentially identical to journal papers that have already been published.

Search Strategy

We used "characteristics and management of gonorrhea." as keywords. The search for studies to be included in the systematic review was carried out using the PubMed and SagePub databases by inputting the words: ("Gonorrhea"/[MeSH Subheading] OR "Infection of gonorrhea"/[All Fields] OR "Characteristics of gonorrhea" [All Fields]) AND ("Risk of

gonorrhoea"[All Fields] OR " Management of gonorrhoea "[All Fields]) AND ("Sign of gonorrhoea"[All Fields]) OR ("Complications of gonorrhoea" [All Fields])) used in searching the literature.

Data retrieval

After reading the abstract and the title of each study, the writers performed an examination to determine whether or not the study satisfied the inclusion criteria. The writers then decided which previous research they wanted to utilise as sources for their article and selected those studies. After looking at a number of different research, which all seemed to point to the same trend, this conclusion was drawn. All submissions need to be written in English and cannot have been seen anywhere else.

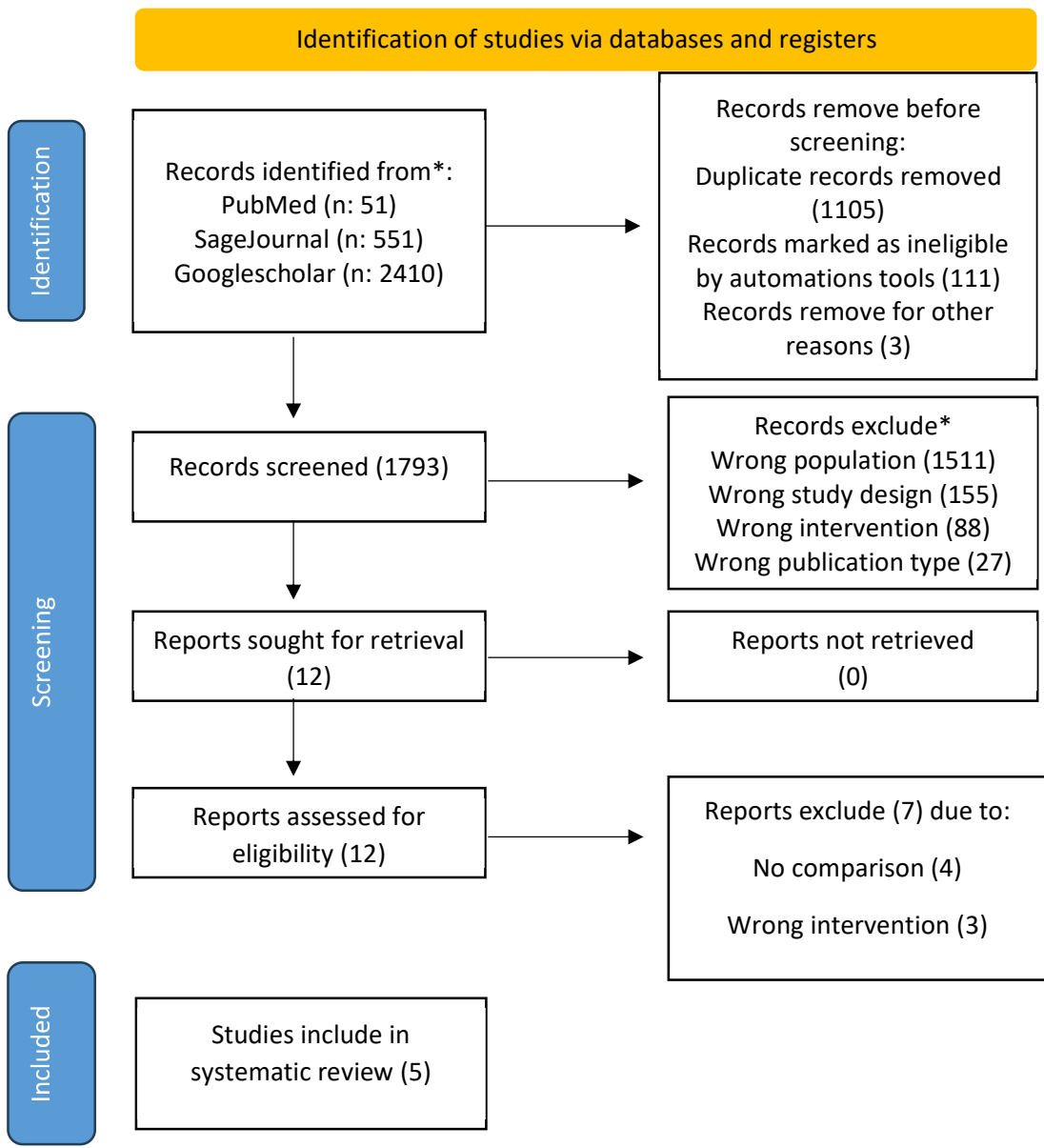


Figure 1. Article search flowchart

Only those papers that were able to satisfy all of the inclusion criteria were taken into consideration for the systematic review. This reduces the number of results to only those that are pertinent to the search. We do not take into consideration the conclusions of any study that does not satisfy our requirements. After this, the findings of the research will be analysed in great detail. The following pieces of information were uncovered as a result of the inquiry that was carried out for the purpose of this study: names, authors, publication dates, location, study activities, and parameters.

Quality Assessment and Data Synthesis

Each author did their own study on the research that was included in the publication's title and abstract before making a decision about which publications to explore further. The next step will be to evaluate all of the articles that are suitable

for inclusion in the review because they match the criteria set forth for that purpose in the review. After that, we'll determine which articles to include in the review depending on the findings that we've uncovered. This criteria is utilised in the process of selecting papers for further assessment. In order to simplify the process as much as feasible when selecting papers to evaluate. Which earlier investigations were carried out, and what elements of those studies made it appropriate to include them in the review, are being discussed here.

RESULT

From the PubMed database, the results of our search get 51 articles, whereas the results of our search on SagePub get 551 articles, on Google Scholar 2410 articles. Records remove before screening are 1219, so we get 1793 articles for screening. After we screened based on record exclude, we compiled a total of 12 papers. We included five research that met the criteria.

Boiko, I et al (2020)⁷ showed the management of *N. gonorrhoeae* infection in Ukraine are the low level of examined females, asymptomatic infection in patients and sexual partners; disregarded testing of extragenital specimens, using of conventional laboratory tests (microscopy and culture) for screening and diagnostics of gonorrhea; deficient access to nucleic acid amplification tests in the public leading specialised STI clinics in Ukraine, low level of screening for HIV; low compliance of the follow-up visits; receiving questionable or even obsolete antimicrobial treatment. It is also supposed by our data that gonococcal infection is stigmatised. Therefore, more accurate and comprehensive management of gonorrhoea is urgently needed in Ukraine.

Budkaew, J et al (2019)⁸ showed the most common site of gonorrhoea infection was male genital site, and the independent risk factors for male genital gonorrhoea were history of diagnosed STDs and having more than one partner in the past 3 months. On the other hand, 100% condom use was a protective factor of gonorrhoea infection in a person. There is needed for increased emphasis on gonorrhoeal infection screening in all three anatomic sites, among asymptomatic MSM. The NAATs method should be implemented in our setting for higher rate detection of gonorrhoea. Health education promoting regular condom use should be continued to prevent risk of gonorrhoea infection in populations with risky behavior.

Table 1. The literature include in this study

Author	Origin	Method	Sample Size	Result
Boiko, I et al., 2020⁷	Ukraine	A retrospective descriptive study of the medical records of 136 adult patients with gonorrhoea that visited Ternopil Regional Sexually Transmitted Infections Clinic (Ukraine) in 2013-2018 was performed.	400	The male-to-female ratio was 6.6:1. Homosexually-acquired gonorrhoea was 3.7%. Also, most patients acquired gonorrhoea in Ukraine (98.4%). The mean infectious period lasted 2-16 days, including the incubation period of 1-9 days and the period from the onset of symptoms to the first visit of the clinic of 1-7 days. The probability of <i>N. gonorrhoeae</i> transmission within the frame of the epidemiologic sexual chain was 1:2.4. Concurrent <i>T. vaginalis</i> (39.7%) and <i>C. trachomatis</i> (2.2%) were detected. HIV and syphilis screening rates were 1.6% and 0.7%, respectively. The examining rate of sexual partners was 11%, testing extragenital specimens - 0.7%, screening coverage for HIV - 46.3%, compliance with follow-up visits - 41.9%. Part of patients (16.2%) received monotherapy with clarithromycin, doxycycline, benzylpenicillin, azithromycin, or ofloxacin.
Budkaew, J et al., 2019⁸	Thailand	We have conducted a cross-sectional	358	One hundred and ninety-five out of 358 (54.47%) MSM tested were found to be

		analysis of a sexually transmitted disease (STD), gonorrhea among MSM attending two STD clinics in Khon Kaen, Thailand.		positive for gonorrhea using a porA gene targeted NAAT by Real-time PCR with TaqMan probes, but there was no positive result by culture. The gonorrheal prevalence for male genital site, anal, and oropharyngeal, were 34.73% (95%CI 33.07, 45.08), 29.01% (95%CI 24.61, 34.33), and 27.93% (95%CI 23.35, 32.89), respectively, while 5.9% (21/355) were positive for gonococcal infection in all anatomic sites (oropharynx + anus + urethra) of one participant. Previous history of diagnosed STDs was a significant factor associated urethral gonorrhea (odds ratio = 3.52, 95%CI 1.87–6.66, P Value < 0.001). In addition, having more than one partner was increased urethral gonorrhea (adjusted odds ratio = 2.26, 95%CI 1.10–4.68, P Value = 0.026). 100% of condom use was found decreasing urethral infection (adjusted odds ratio = 0.39, 95%CI 0.15–0.99, P Value = 0.046).
Findlater, L et al., 2021⁹	UK	A modelling study.	8013	Between 2015 and 2017, 8013 isolates were collected: 64% from men who have sex with men, 18% from heterosexual men and 18% from women. Across participant subgroups, stratified by all predictors, resistance prevalence was high for ciprofloxacin (range: 11%–51%) and penicillin (range: 6%–33%). Resistance prevalence for azithromycin and cefixime ranged from 0% to 13% and for ceftriaxone it was 0%. Simulating model use, 88% of individuals could be given cefixime and 10% azithromycin, saving 97% of ceftriaxone doses, with 1% of individuals delayed effective treatment.
Yeshanew, AG et al., 2018¹⁰	Ethiopia	A cross-sectional study was conducted from April 1 to August 30, 2016 in Gondar town hospitals and health centers, Gondar town,	120	The antimicrobial susceptibility pattern of all isolates of <i>N. gonorrhoeae</i> . All isolates of <i>N. gonorrhoeae</i> showed resistance to at least one antimicrobial agent. The susceptibility pattern of isolates shows there were a hundred percent non-susceptibility for tetracycline,

		Northwest Ethiopia.		76% non-susceptibility and 24% intermediate resistant for penicillin. The isolated <i>N. gonorrhoeae</i> was resistant 52% to ciprofloxacin, 48% to ceftriaxone, 44% to cefoxitin, 29% to cefotaxime, and 28% to clindmycin. Most of the isolates (80%) showed multiple drug resistance and 11(44%) of the isolates showed non-susceptibility to both ciprofloxacin and ceftriaxone.
Yaesoubi, R et al., 2020 ¹¹	USA	We developed and calibrated a mathematical model of gonorrhea transmission among men who have sex with men (MSM) in the United States. We calibrated the model to the estimated prevalence of gonorrhea, the rate of gonorrhea cases, and the proportion of cases presenting symptoms among MSM in the US.	5000	The tradeoff between increasing the effective life span of antibiotics and reducing the annual incidence of gonorrhea. The origin in this figure represents the status quo, in which switching policies are triggered when greater than 5% of the isolates tested are resistant. Increasing this resistance-prevalence threshold for switching to new antibiotic drugs (moving toward the top-right corner of increases the effective life span of drugs A and B by using the existing drugs for a longer period. Increasing this switching threshold, however, leads to increases in the expected number of annual gonorrhea cases because delaying the switch to a new antibiotic drug lowers the probability of receiving an effective first-line therapy, thereby extending the expected duration of infectiousness while these cases await detection of treatment failure and treatment with effective second-line therapy.

Findlater, L et al (2021)⁹ showed substituting ceftriaxone for cefixime in the majority of patients would be undesirable as it could prompt the return of widespread cefixime resistance and potentially also select for ceftriaxone resistance, while widespread use of azithromycin monotherapy also risks the return of azithromycin resistance. Therefore, the analysis suggests that there may not be enough variation in patient susceptibility to these antibiotics for this approach to be feasible in the current context.

Yeshanew, AG et al (2018)¹⁰ showed high prevalence of *N. gonorrhoeae* and drug resistance among symptomatic clients who attended the STI clinics in the study area was observed. This should cause alarm and should lead to a large community based study and increased awareness of both regional health bureaus and the Ministry of Health about the treatment guidelines.

Yaesoubi, R et al (2020)¹¹ showed while we await a breakthrough (new antimicrobial agents, novel molecular assays to determine susceptibility to antimicrobial agents, or a gonococcal vaccine), it is important to optimize the use of surveillance systems to minimize the burden of gonorrhea and to slow the spread of antibiotic-resistant strains. We demonstrated the potential for data from surveillance programs to be used in a more efficient and active way to prolong the effective life spans of existing antibiotics without increasing the burden of the disease.

DISCUSSION

Gonorrhoea, a sexually transmitted infection, is the second most commonly reported notifiable disease in the United States, with a total of 333 004 new cases reported to the Centers of Disease Control and Prevention (CDC) in 2013. However, because many infections are never diagnosed or reported, the true burden of gonococcal infection is likely significantly higher. It is estimated that >800 000 new gonococcal infections occur in the United States each year.¹²

Although the national gonorrhoea rate has declined substantially from its peak in 1975 (464.1 cases per 100 000 population) and reached an all-time low in 2009 (98.1 cases per 100 000), the rate subsequently increased each year during 2010–2012, and plateaued at 106.1 cases per 100 000 population in 2013. High gonorrhoea rates continue to be observed in certain demographic groups and geographic areas. In particular, adolescents aged 15–19 years (337.5 cases per 100 000 population), young adults aged 20–24 years (500.5 cases per 100 000 population), non-Hispanic blacks (426.6 cases per 100 000 population), and residents of the Southern United States (128.6 cases per 100 000 population) bear the highest burden of disease.¹³

The natural history of untreated gonococcal infection is spontaneous resolution and microbiological clearance after weeks or months of unpleasant symptoms. During this time, there is a substantial likelihood of transmission to others and of complications developing in the infected individual. In many women, the lack of readily discernible signs or symptoms of cervicitis means that infections go unrecognised and untreated. An unknown proportion of untreated infections causes local complications, including lymphangitis, periurethral abscess, Bartholinitis, and urethral stricture; epididymitis in men; and, in women, involvement of the uterus, fallopian tubes, or ovaries causing pelvic inflammatory disease (see review on Pelvic inflammatory disease).^{14,15}

Unfortunately, *Neisseria gonorrhoeae* has developed resistance to all antimicrobials introduced for treatment of gonorrhoea since the mid-1930s, when sulphonamides were introduced. The resistance to many antimicrobials has also rapidly, within only 1–2 decades, emerged and spread internationally. The bacterium has utilized mainly all known mechanisms of antimicrobial resistance (AMR): inactivation of the antimicrobial, alteration of antimicrobial targets, increased export (e.g., through efflux pumps such as MtrCDE) and decreased uptake (e.g. through porins such as PorB).¹⁶

The mechanisms that change the permeability of the gonococcal cell are particularly concerning because these decrease the susceptibility to a wide range of antimicrobials with different modes of action, e.g., penicillins, cephalosporins, tetracyclines and macrolides. At present, the prevalence of *N. gonorrhoeae* resistance to most antimicrobials earlier recommended for treatment worldwide, such as sulphonamides, penicillins, earlier generation cephalosporins, tetracyclines, macrolides and fluoroquinolones, is high internationally. In most countries, the only options for first-line empirical antimicrobial monotherapy are currently the extended-spectrum cephalosporins (ESCs) cefixime (oral) and particularly the more potent ceftriaxone (injectable).¹⁷

CONCLUSION

The management of *N. gonorrhoeae* infections was compromised by a low rate of examining sexual partners, females and testing extragenital specimens, screening for HIV, compliance to follow-up visits, access to nucleic acid amplification tests, and receiving questionable or even obsolete antimicrobial treatment. Therefore, more accurate and comprehensive management of gonorrhoea is urgently needed.

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