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International Journal of Medical Science and Dental Health (ISSN: 2454-4191)
Volume 11, Issue 06, June 2025,
Doi https://doi.org/10.55640/ijmsdh-11-06-19

Pathogenesis And Antibiotic Resistance of Neisseria Gonorrhoeae: A Review Article

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Received: 24 April 2025, **accepted:** 31 May 2025, **Published Date:** 26 June 2025

ABSTRACT

Neisseria gonorrhoeae is a major public health problem. Rising prevalence and increasing antibiotic resistance in this organism make a growing concern. Timely treatment and management of infections depend on better understanding its microbiological features and effective diagnostic methodologies. Neisseria gonorrhoeae, the etiologic agent of gonorrhea, is an important sexually transmitted infection (STI). The pathophysiology of infections due to N. gonorrhoeae describes interaction of the bacterium with host defense mechanisms that result in various clinical manifestations. Neisseria gonorrhoeae has almost continuously over the last decades been a significant public health challenge increasing infection rates and rising antibiotic resistance. Hence updated protocols for therapy as recently guidelines recommended based upon research findings. This paper shall carry an integrative appraisal of recent works related to the microbiological traits of N. gonorrhoeae, the competence of current diagnostic measures, and the menace brought by antimicrobial resistance. It carries an integrative appraisal of existing research findings on the pathogenesis of N. gonorrhoeae with a focus on its infection mechanisms, antimicrobial resistance, and implications for treatment. This paper shall carry another integrative appraisal of existing perceptions concerning the antimicrobial treatment of infections caused by N. gonorrhoeae with a focus on challenges from patterns of resistance, adequacy levels of existing regimens, and possible future directions in research.

KEYWORDS

Pathogenesis, treatment approaches, Neisseria gonorrhea

INTRODUCTION

Recent studies show N. gonorrhoeae at extragenital sites, mostly in men who have sex with men (MSM). As sites are often asymptomatic, diagnosis is challenging and may also facilitate further transmission (Chan et al., 2016). Extragenital infections are asymptomatic, hence effective screening practices should be implemented to pick out those infections that usually go unnoticed especially among high-risk populations .

Antibiotic resistance in Neisseria gonorrhoeae has thus raised still further alarms within the medical community.

A study assessing the genomic epidemiology of gonococcal resistance with very high levels of resistance to extended-spectrum cephalosporins, macrolides, and fluoroquinolones (Grad et al., 2016). The detection of resistant clones like FC428 clone reported in the UK illustrates this point quite well-urgent need increased surveillance, rapid diagnostic testing that can pick up such strains promptly enough to tailor appropriate therapies (Eyre et al., 2019). Some recent advances in diagnostics do hold promise for detecting N. gonorrhoeae with quite high sensitivity and specificity-Cepheid CT/NG Xpert PCR test at least appears one of them (Gaydos et al., 2013). The more important new tests-at least they help where they are most needed-is resource-limited settings where timely diagnosis can prevent ensuing complications due to untreated gonorrhea. There is-about assessment of extragenital infection screening protocols-still a gap. More development is needed in targeted diagnostic tests (Chan et al., 2016).

Since antibiotic resistance is a growing concern, new treatment options are necessary. Recent research has shown the promising results of zoliflodacin, a next-generation antibiotic, which was effective in curing the majority of cases involving urogenital and rectal infections but incomplete in some cases of pharyngeal infections (Taylor et al., 2018). This emphasizes the demand for rapid diagnostic tests that can detect susceptibility profiles to direct appropriate treatment—an increasing resistance to standard therapy makes this point clear (Rice et al., 2017). Though considerable progress has been made regarding N. gonorrhoeae, certain gaps persist about the lag not only in developing rapid diagnostics at the point of care for detecting resistant strains but also compared to what was happening microbiologically and even with mechanisms of resistance (Cortina et al., 2016) .

Considerable progress has been made in understanding and controlling the transmission of N. gonorrhoeae, yet substantial gaps remain in knowledge. Long-term effectiveness results for combination therapies and data regarding the development of resistance to new drugs, like zoliflodacin and azithromycin, are urgently needed. Further applications of WGS within clinical practice could also improve future capabilities to predict resistance patterns and thus better tailor treatment. More detailed studies on screening practices are warranted given most extragenital infections are asymptomatic-in addition to treatment efficacy in different populations. Future research directions lie as well in the psychosocial factors affecting adherence to treatment among high-risk populations- where a significant number of investigations into N. gonorrhoeae have not closed knowledge gaps (Chisholm et al., 2010).

Moreover, the increase in antibiotic resistance underlines the importance of investigations oriented toward genetic and environmental factors that drive this process. In a future study, more novel therapeutic strategies-that could include alternative antibiotics and combination therapies effective against resistant strains-should be investigated. Another promising field is the modulation by the gut microbiota of the immune response to infection by N. gonorrhoeae, mainly considering the emergent concept on the influence of microbiotas in health and disease (Muscogiuri et al., 2019).

Pathogenesis of Neisseria gonorrhoeae

Neisseria gonorrhoeae infection begins with adherence to mucosal epithelial cells, mainly in the urogenital tract pili and Opa proteins associated with opacity results in adherence (Edwards & Apicella, 2004). After successfully attaching itself to the host cells, invasion ensues and antigenic variation along with resistance complement-mediated killing helps it evade immune responses (Zughaier et al., 2015). These bacteria multiply porin protein inside host cells facilitating survival within the cell. In addition, N. gonorrhoeae strong inflammatory response especially neutrophil infiltration may drive symptomatic disease and at the same time lead tissue damage (Liu et al., 2018). Adaptive immunity against this pathogen is usually not protective and allows for persistence of infection hence reinfection can occur about the ability of this organism to suppress adaptive immune responses. Complex pathogenesis has so far precluded vaccine development but should be considered when planning therapeutics (Rice et al., 2017).

N. gonorrhoeae has developed various virulence factors that facilitate its infection process. The major mechanisms are the adherence to and invasion of epithelial cells mainly in the urogenital tract. Pili mediate this adhesion together with other surface proteins that share interactions with receptors on the host cell, establishing a foothold for the bacterium to cause infection (Unemo & Shafer, 2011). Besides, N.

gonorrhoeae can escape immune responses from hosts through various strategies. For example, it has been demonstrated to manipulate neutrophil responses in the innate immune system. Normally, under infectious conditions, neutrophils produce reactive oxygen species (ROS) as a means of killing the pathogen. But, research shows that N. gonorrhoeae can trigger NADPH oxidase in neutrophils resulting in a contradictory increase in ROS production which may not effectively kill the bacteria (Nguyen et al., 2017). This trick does not just help the germ to live in tough places but also leads to harm to tissues and swelling.

Increasing antibiotic resistance in N. gonorrhoeae poses great challenges for gonococcal infection management. The organism has sequentially developed resistance to multiple classes of antibiotics, such as penicillins, tetracyclines, and fluoroquinolones mainly through genetic mutations and horizontal gene transfer (Unemo & Shafer, 2011). Such mechanisms as beta-lactamase production and drug target modification greatly reduce the efficacy of commonly administered antibiotics. A recent discovery has shown a worrying degree of co-resistance among Gram-negative bacteria, including N. gonorrhoeae that further narrows the choices for effective treatment.How else can this be handled when even some strains have already been detected with carbapenem and aminoglycoside resistance (Unemo & Shafer, 2011)? This presents enormous clinical implications as fewer alternative treatments would translate into increased morbidity and mortality.N.gonorrhoeae infections are not limited to urogenital Ngonococcal infections. N. gonorrhoeae can infect the pharynx and rectum- infections which are often asymptomatic- therefore transmission is most likely to continue (Chan et al., 2016). The pathophysiological mechanisms of extragenital infection are not yet fully understood; future research should clarify both their clinical significance and appropriate management.

Antibiotic Resistance

Neisseria gonorrhoeae is increasingly resistant to antibiotics in a growing number of classes and poses a significant threat to global public health. This bug has over the last several decades progressively gained resistance to penicillin, tetracycline, and fluoroquinolones, and more recently decreased susceptibility to third-generation cephalosporins-including ceftriaxone which is now the only readily available injectable treatment option (Unemo & Shafer, 2014). Multidrug resistance strains further compound limited treatment options with increased challenges to control strategies (Wi et al., 2017). Such mechanisms as β-lactamase production, efflux pumps, and target site mutations are responsible (Lewis, 2013). The surveillance data that have been so far reported reflect these MIC creepingly alarming trends worldwide particularly in high burden regions. Thus calls urgently for new antimicrobials plus improved global systems for monitoring resistance (WHO, 2021).

The development of antimicrobial resistance by N. gonorrhoeae has been documented, and the principal declines in susceptibility are to the main antibiotics, particularly cefixime (Unemo & Shafer, 2014). Increasing MICs raises concerns about possible treatment failures; thus, active surveillance of resistance trends is needed (Agarwal et al., 2018). Studies already put near enough limits for today's antibiotics to keep up effective treatment protocols that have to be reevaluated for available options (Unemo et al., 2016). Therefore, insufficient sensitivity to cefixime remains a disturbing finding not least because it complicates therapy recommendations and hence carries an increased risk of clinical failure (Agarwal et al., 2018). The rising proportions of extragenital infections caused by N. gonorrhoeae decrease the chances for adequate treatment since those extragenital infections are asymptomatic and require extensive testing; therefore, an individualized approach would be necessary (Chan et al., 2016).

Over the years, the CDC has developed a number of guidelines in response to increasing gonorrhea rates and multiaxial antimicrobial resistance. The 2015 Guidelines for N. gonorrhoeae Treatment shared Additional Regimens of Treatment for N. gonorrhoeae in which they recognized this urgent need to respond effectively to antimicrobial resistance (Workowski & Bolan, 2015). Updates made in 2021 reiterate that treatment recommendations must continue to change with new data on drug efficacy (Workowski et al., 2021).

The major change in treatment regimen is that combination therapy with ceftriaxone and azithromycin has been recommended. This implies an escalated adaptive approach to less susceptibility of gonococci to cefixime and underscores the need for continuous surveillance as well as periodic updating of treatment

guidelines (Kirkcaldy et al., 2012). Such combined treatments are also needed by making the treatments more effective and hence lowering possible resistance that can be developed against them. Targeted screening and management strategies for high-risk populations, particularly men who have sex with men (MSM), would be appropriate for effective control of gonorrhea. The frequency of testing has once again been updated in an adaptive management style for STIs in this population so that healthcare providers can respond adequately to the particular challenges encountered with MSM (Eyre et al., 2017).

The addition of whole genome sequencing (WGS) as a method for predicting antimicrobial susceptibilities in N. gonorrhoeae is the optimistic future in the more precise use of antibiotics on the basis of resistance patterns. This new approach would further improve personalized treatment options, critical to manage increasing resistance and to properly control gonorrhea infection (Allen et al., 2013). Zoliflodacin is an innovation toward compounds targeting resistant strains of N. gonorrhoeae, thus underscoring the need for new therapeutic options in increased resistance (Chisholm et al., 2010). The critical trials that have been initiated on zoliflodacin results have henceforth opened a window of optimism that this compound will be treatment means on drug-resistant gonorrhea thus bringing better treatment results.

CONCLUSION

The microbiological characteristics of Neisseria gonorrhoeae and its diagnostic methodologies are areas that require constant attention. More so, as the landscape of treatment for gonorrhea shifts because of increasing resistance to antibiotics, there is a need for improved diagnostics and new treatment options. Filling these gaps will substantially enhance public health outcomes in managing the disease. Pathophysiology presents N. gonorrhoeae infections with complicated mechanisms both as regards infection and resistance to existing paradigms of treatment; hence, more fastidious in their exigencies from an interdisciplinary research and clinical perspective between investigators and clinicians. Thus informed interventions through further studies will be helpful in combating this persistent infection. Increasingly, though, systems managing infections caused by N. gonorrhoeae do face challenges from antimicrobial resistance directed against previously usable antibiotics compounded by high-risk populations. Continuous updates to the guidelines, with new data and approaches, are needed in the fight against this public health menace. The future research thrust should be on filling up existing knowledge gaps and building strategies to improve treatment outcomes under evolving resistance patterns.

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