

Special Article: Sexually Transmitted Infections

Multidrug-Resistant *Neisseria Gonorrhoeae* Infection**Abhishek Lachyan¹; Pragyana Swagatika Panda²; Sumathi Muralidhar^{1*}; Niti Khunger³**¹Apex Regional STD Centre & SRL-HIV, Safdarjung Hospital, New Delhi, India²Department of Microbiology, Vardhaman Medical College Hospital, Safdarjung Hospital, New Delhi 110029, India³Head of Department, Department of Dermatology & STD and Apex Regional STD Centre, Safdarjung Hospital, New Delhi, India***Corresponding author: Dr. Sumathi Muralidhar**

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Gonorrhoea, an important Sexually Transmitted Infection (STI), continues to pose a significant public health challenge. According to estimations by the World Health Organization (WHO), there were approximately 82.4 million new cases of this infection among adolescents and adults aged 15-49 years in 2020, with a global incidence rate ranging from 11-29 per 1000 women and 10-43 per 1000 men [1,2]. Most cases were reported in the WHO African and Western Pacific regions. This data underscores the necessity for increased efforts to address the problem of gonorrhoea on a global scale [3].

To achieve a thorough understanding and reduction of antimicrobial resistance in *Neisseria gonorrhoeae*, it is essential to improve and implement effective measures for gonorrhoea prevention and management. Additionally, it is of paramount importance to delve into the intricacies and mechanisms of drug resistance in *Neisseria gonorrhoeae* and study its fundamental aspects, including its causes, prevalence, and mechanisms of drug action. Such a comprehensive approach will enable healthcare practitioners to mitigate the risks of antimicrobial resistance and safeguard public health, particularly sexual health.

The emergence and spread of Antimicrobial Resistance (AMR) in *Neisseria gonorrhoeae* (*N. gonorrhoeae*) had its beginnings at least eight decades ago, affecting the efficacy of several drugs including tetracyclines, sulphonamides-trimethoprim

combinations, quinolones (ciprofloxacin), and, most recently, macrolides (azithromycin), all of which were one-time drugs of choice in the treatment of gonorrhoea. In several nations, including India, there is an alarmingly high rate of ciprofloxacin resistance. Azithromycin resistance is an emerging issue, and resistance or diminished susceptibility to Cefixime and Ceftriaxone is also a matter of concern [1]. In 2009, two definitions were put forth to describe the Multi-Drug-Resistant *Neisseria Gonorrhoeae*. The multi-drug-resistant gonococcus (MDR-GC) is one that shows decreased susceptibility or resistance to one currently recommended therapy (cephalosporin or azithromycin), plus resistance to at least two other antimicrobials used for gonorrhoea. Extensively drug-resistant gonococcus (XDR-GC) is one that shows decreased susceptibility or resistance to two currently recommended therapies (cephalosporin and azithromycin), plus resistance to at least two other antimicrobials used for gonorrhoea (penicillin, tetracycline, erythromycin, ciprofloxacin) [2].

The initial incidence of treatment ineffectiveness with cefixime was first observed in Japan. However, over the last decade, instances of verified inability to cure gonorrhoea with ceftriaxone as a standalone treatment or in combination with azithromycin or doxycycline have been documented in multiple countries, including Australia, France, Japan, Slovenia, Sweden, the United Kingdom, or Great Britain and Northern Ireland. The

ability of *N. gonorrhoeae* to resist a wide range of treatment options, including penicillins, sulphonamides, tetracyclines, quinolones, macrolides, and even the class of cephalosporins, typically reserved as a last resort, renders this pathogen a formidable multidrug-resistant organism, or a superbug status. Gonococcal infections carry significant consequences for reproductive, maternal, and neonatal health. Notably, they can result in a quintupling of HIV transmission rates and infertility, which can have substantial cultural and societal impacts. Additionally, inflammation caused by these infections can lead to acute and chronic lower abdominal pain in women, ectopic pregnancy, first-trimester abortions, and maternal mortality. Finally, severe neonatal eye infections may occur (ophthalmia neonatorum), posing a risk of blindness in affected infants [4].

The effective management of multidrug-resistant *N. gonorrhoeae* necessitates a dual approach, encompassing broad control of drug resistance and the gonorrhea infection itself. It is imperative that both of these approaches are undertaken within the broader scope of global antimicrobial resistance control. To this end, the World Health Organization is currently executing the Global Action Plan to Control the Spread and Impact of Antimicrobial Resistance in *N. gonorrhoeae*, which seeks to facilitate efficacious action against the dissemination of multidrug-resistant strains of *N. gonorrhoeae*. This plan forms an integral component of the wider STI surveillance strategy, which aims to enable the early identification of emerging resistant strains while simultaneously implementing a public health response to prevent and treat gonococcal infections and minimize the impact of gonorrhea on sexual and reproductive health.

The Global Health Sector Strategy on HIV, Hepatitis, and STIs (2022-2030) has established ambitious targets aimed at mitigating the prevalence of gonorrhea among individuals aged between 15 and 49 years. The objective entails a drastic reduction in the number of new cases from 82.3 million per annum in 2020 to 8.23 million per annum by 2030, constituting a 90% drop in incidence by the end of the decade. Nonetheless, the strategy recognizes that achieving this reduction may be arduous, given the current interventions and the escalating antimicrobial resistance. Consequently, the strategy underscores the need to develop effective gonococcal vaccines since none exist currently. The pressing need for gonococcal vaccine development has been galvanized by the escalating gonococcal antimicrobial resistance and the mounting scientific evidence supporting the biological viability of such vaccines [5].

To address the issues of preventing and controlling gonococcal infections, it is crucial to disseminate awareness on prevention interventions and administer appropriate treatment regimens. Furthermore, it is imperative to establish potent drug regulations to facilitate effective treatment outcomes. To combat antimicrobial resistance, especially in countries with high burdens of gonococcal infections, surveillance systems must be fortified, and the number of countries reporting antimicrobial resistance in *N. gonorrhoeae* to the WHO Gonococcal Antimicrobial Surveillance Programme (GASP) must be amplified from 36% in 2020 to over 70% by 2030. The Gonococcal Antimicrobial Surveillance Programme must be reinforced by creating a network of laboratories carrying out gonococcal antimicrobial resistance surveillance that are linked to the Global Antimicrobial Resistance and Use Surveillance System. Additionally, regional networks of laboratories that can perform gonococcal culture and drug susceptibility testing with reliable quality control mechanisms need to be established [5].

Author Statements

Conflicts of Interest

The authors declare no conflicts of interest.

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