

## The Public Health Perspective of Gonococcal Infection in Neonates

Dear Editor,

*Neisseria gonorrhoea* is the second most prevalent sexually transmitted infection (STI), and World Health Organisation (WHO) estimates that in 2020, there are 82.4 million [47.7 million-130.4 million] new cases infected among adolescents and adults aged 15–49 years worldwide.<sup>[1]</sup> Most cases were in the WHO African region and the Western Pacific region. The cases are continuously increasing in several countries when compared to the past decade. Notably, the infection rates are considerably higher in developing and low-middle income countries than the developed countries owing to the unavailability of screening and treatment options. Although various bacterial and viral agents cause neonatal septic conjunctivitis, *N. gonorrhoea* is the most common pathogen that threatens the eye vision, if left untreated; it may lead to permanent blindness and associated mortality. The estimates show that gonococcal conjunctivitis (GC) remains a significant cause of childhood corneal blindness in developing countries. Notably, the disease prevalence of GC is high in women, i.e. 0.9%, compared to men, i.e., 0.7%. The annual estimate shows the varied infection rate across the globe ranging from 0.08 to 7% in pregnant women and 0.06 to 0.4% in neonates.<sup>[2]</sup> It is estimated that about 50% of neonates born from *N. gonorrhoea* infected mothers will develop GC. This is majorly because of the asymptomatic nature of the disease among 80% of pregnant women.<sup>[3]</sup>

*Neisseria gonorrhoea* is still posing as public health challenge in India with prevalence ranging from 0 to 22% and rising antibiotic resistance against commonly used antibiotics.<sup>[4]</sup> Various studies conducted in different parts of India reported high prevalence of gonorrhoea among HIV positive and 20–30 years of age group with male preponderance and risk factors such as low socio-economic status, unmarried, multiple sexual partners, living in urban area, profession involving long stay away from home, and past history of STI found to be associated with high prevalence of gonorrhoea.<sup>[5,6]</sup>

Not only in neonates, gonococcal infections in pregnancy can cause complications like fatal loss, premature rupture of membranes, low birth weight, preterm labor and delivery, and chorioamnionitis. Following the infection in neonates, this bacterium attaches to the epithelial cells of the mucosal surface of the conjunctiva. However, recent evidence shows that this pathogen has evolved to escape from the immune responses, which could lead to potential systemic infections such as stomatitis, rhinitis, arthritis, bacteraemia, and meningitis.<sup>[7]</sup> Although this neonatal infection has decreased globally, the consequences of the untreated disease remain severe while

considering the increasing prevalence of *N. gonorrhoea* globally, especially in women.<sup>[3]</sup>

GC in neonates can be initially identified by symptoms such as red eyes, swelling of eyelids, and profuse purulent discharge. Further to confirm the occurrence of *N. gonorrhoea*, conjunctival scraping, and exudative fluid samples from the suspected cases are being collected for the following diagnostic procedures 1) the Gram staining, which is the predictive test for the etiological agent of GC, 2) the culture-based diagnostic approaches, and 3) transcription-mediated amplification test and Polymerase Chain Reaction test will be more sensitive than culture-based for detecting *N. gonorrhoea*.

Preliminarily, regular (1 to 2 hours) topical irrigation with normal saline to remove profuse mucopurulent or purulent eye discharge will be preferred. Followed by this, ophthalmic ointment of erythromycin or tetracycline will be given. However, local antimicrobial liniments are alone ineffective, and it is not desirable when systemic antibiotic therapy is administered. Moreover, erythromycin resistances emerging throughout the globe, which made it ineffective of using this first-line treatment. On the other hand, systemic administration of antibiotic therapy is considered an effective mode of treatment in neonates with GC. As per the WHO guidelines, neonates can be given with either of the following with intramuscular as a single dose 1) ceftriaxone 25 to 50 mg/kg (max 150 mg), 2) kanamycin 25 mg/kg (max 75 mg) and spectinomycin 25 mg/kg (max 75 mg).<sup>[8]</sup> However, neonates with hyper bilirubinemia or those receiving calcium-containing fluids should be neglected for ceftriaxone. In addition, cefotaxime (100 mg/kg IV/IM) can be given as a single dose. Moreover, sulfonamides, penicillins, tetracyclines, macrolides, and fluoroquinolones are no longer options for empirical treatment due to the high percentage of resistance detected worldwide. The emerging resistance against fluoroquinolones is the reason why cephalosporins are used in the *N. Gonorrhoea* treatment currently. In addition to these innervations, new-born must be evaluated for conditions such as arthritis, meningitis, sepsis, and anorectal infection, although rare.

Topical ocular prophylaxis is the recommended treatment option for neonates having more chance to acquire the infection.<sup>[8]</sup> Topical prophylactic treatment such as 1% silver nitrate is used to cure GC in neonates. In addition, other preferences such as erythromycin (0.5%), povidone-iodine (2.5%), tetracycline hydrochloride (1%), and chloramphenicol (1%) effectively prevent gonococcal infection after delivery, whether it is vaginal or caesarean. Neonates of mothers having gonorrhoea must have a single dose of ceftriaxone as recommended

above. However, there is no systematic prophylaxis to treat GC in neonates.

Considering these clinical complications of neonatal GC, the most effective treatment is prevention for several reasons. The following are the few strategies, which may be helpful to prevent and control neonatal gonococcal transmission and thereby their prevalence in future.

- **Vaccination against Gonorrhoea:** Vaccination is an age old proven technique to curb any epidemic or pandemic. It is need of time for safe and effective vaccine against gonococcal infections when there is emergence of multidrug-resistant *N. gonorrhoeae* strains and limited treatment options available against it. Even after 50 years of research, vaccine development for gonorrhoea is still in the preclinical phase and only three vaccine candidates have progressed to clinical trials.<sup>[9]</sup> The evaluation of vaccine candidates has been challenging because no correlates of protection have been identified against *N. gonorrhoeae* in humans. The development of successful vaccine against *N. gonorrhoeae* will be game changer as it was estimated that a 90% reduction in gonorrhoea prevalence could be achieved in 20 years if a non-waning gonococcal vaccine of 50% effectiveness (or a 100% efficacy vaccine that wanes after 7.5 years) is administered to all 13 year olds in a model-based epidemiological simulation study.<sup>[10]</sup>
- **Advocacy for adopting behavior modification:** High-risk behavior groups (especially HIV infected, history of STIs, and high-risk sexual behavior) must adopt and promote their partners for behavioral modification such as using condoms, periodical screening for STIs, and prophylaxis therapy to prevent the transmission.
- **Exploration of the history of high-risk behavior:** Clinicians are advised to have an effective discussion with pregnant women as well as their sex partners about any high-risk sexual behavior (if any) and unusual symptoms they are experiencing currently or in the past.
- **Screening of pregnant women:** Screening of all women (belonging to the high-risk group) at their first prenatal visit and treatment of gonococcal infections, if detected during pregnancy, is highly recommended.
- **Public health strategies as per disease prevalence:** Since prenatal screening and treatment of pregnant women are effective strategies for preventing and controlling GC, countries experiencing high prevalence must adopt such strategies to mitigate gonococcal transmission and neonatal mortality.
- **Treatment of partner (s) and exploration of other STI infections:** The presence of neonatal GC indirectly indicates the infectious status of their parents. Thus, they must be screened with other sexually transmitted infections such as human immunodeficiency virus, Hepatitis A, Hepatitis B, Human Papilloma Virus, and syphilis; if detected, immediate treatment measures should be promoted.

- **Search for new therapies:** The rapid elimination of colonizing gonococci upon delivery through effective topical prophylaxis would be the left option for treating neonates with multi-drug resistance strain. In addition, efforts should be made to explore novel therapeutic molecules (i.e., monocaprin).

Thus, apart from following the above mentioned strategies, we need to work in future on the following few crucial aspects: all infants must be protected from the transmission of all kinds of bacterial and viral pathos from mother; antibiotics should be free from the side effects of existing topical treatment like chemical conjunctivitis, and treatment should preferably be available in single-dose episodes; as resistance has been estimated to increase, development of effective vaccine should be of high priority. Therefore, all these interventional approaches along with the behavioral change should be envisaged as an ideal prophylactic and treatment of GC, and it will provide a colorful world to the children.

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### Conflicts of interest

There are no conflicts of interest.

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