Antimicrobial susceptibility of *N. gonorrhoeae* in Bangladesh: 2014 update

Rasheda Khanam\(^a,b\), Dilruba Ahmed\(^a\), Mustafizur Rahman\(^a\), M. S. Alam\(^a\), Mausumi Amin\(^c\),
Sharful Islam Khan\(^a\), Kenneth H. Mayer\(^d\), Tasnim Azima

International Centre for Diarrhoeal Disease Research, Bangladesh (icddr,b), Dhaka, Bangladesh\(^a\)
International Center for Maternal and Newborn Health, Department of International Health,
Johns Hopkins Bloomberg School of Public Health, Baltimore, Maryland, USA\(^b\)
Save the Children Dhaka, Bangladesh\(^c\)
Fenway Institute, Beth Israel Deaconess Medical Center, Harvard Medical School, Boston,
USA\(^d\)

*Communicating author: Mustafizur Rahman\(^a\), mustafizur@icddrb.org*
Documentation of *N. gonorrhoeae* resistance to multiple antibiotics globally has given rise to major concerns regarding a future of untreatable gonorrhea (1, 2). In Bangladesh, *N. gonorrhoeae* antimicrobial susceptibility was last examined between 1997-2006 in female sex workers (FSW), male having sex with male (MSM), patients with sexually transmitted infections (STI) and truckers and resistance to ciprofloxacin, penicillin and tetracycline with reduced susceptibility to cefixime as well as multidrug resistance were reported (3, 4, 5). The present analysis was conducted to update this data so as to inform guidelines on syndromic management of sexually transmitted infections (STIs) developed in 2006 (6) that are currently being used in Bangladesh, and to enhance global surveillance by the World Health Organisation.

The current report presents data on antimicrobial resistance of *N. gonorrhoeae* from a cross-sectional bio-behavioral survey of STIs conducted among key populations (KPs) at risk of HIV in Dhaka, Bangladesh between August and November 2014. The KPs included FSW (N=700), females who injected drugs (FWID) (N=177), male sex workers (MSW, N=227) and transgender women known as Hijras (N=169). All were adults (>18 years) and were enrolled on a first come, first served basis from drop in centers (DICs) under the Global Fund Program for HIV which provides STI prevention services to enlisted KPs. Individuals were enrolled only if they provided written informed consent for their participation in the study. The study was approved by the Research and Ethical Review Committees of icddr,b.

Study physicians conducted physical examination and collected cervical swabs under speculum examination (FSW and FWID) and anorectal swabs (MSW and Hijras) using aseptic techniques. All swabs were transported to icddr,b in Ameis charcoal transport media within 6-8 hours of collection. Swabs were cultured for identification of *N. gonorrhoeae* and antibiotic susceptibility.
testing were carried out for positive isolates. Anorectal swabs were directly inoculated onto Modified Thayer Martin (MTM) agar containing vancomycin, colistin, nystatin and trimethoprim. Cervical swabs were inoculated onto MTM agar, blood agar, and chocolate agar media. After inoculation all plates were incubated under microaerophilic conditions (5% O₂) at 35°C for at least 48 hours. The identity of *N. gonorrhoeae* was confirmed by gram stain, oxidase test and Neisseria sugar test (carbohydrate degradation test). Antimicrobial susceptibility testing (AST) was performed by Kirby Bauer method (disc diffusion) and breakpoints of sensitive, intermediate and resistant were interpreted following Clinical and Laboratory Standards Institute (CLSI) guideline (7) and *N. gonorrhoeae* reference strain ATCC 49226 was used as a standard.

Of the 1273 samples, 21 (five anorectal and 16 cervical) tested positive for *N. gonorrhoeae* by culture. This low isolation rate (1.6%) can be explained by the fact that antibiotics were frequently given to our study participants through the HIV/STI prevention program that might have caused a reduction in the bacterial load such that it was undetectable in culture. All *N. gonorrhoea* cultures were tested for AST and the results are shown in Table 1. Ceftriaxone and spectinomycin were the antibiotics to which all isolates were susceptible. The next most sensitive antibiotic was azithromycin (90.5%), followed by cefixime (85.7%). None of the isolates were sensitive to ciprofloxacin, to which resistance was found in 95.2% and intermediate resistance in 4.8% of isolates. More than 90% of the isolates were resistant to doxycycline. Multidrug resistance (against three or more antibacterial agents) was identified in 48% of isolates. Antibiotic resistance data obtained from this study are comparable to data from an earlier study (5).
In this study all participants diagnosed with STIs were provided treatment using the national STI management guideline. The possibility of treatment failure remains given the antimicrobial resistance profile.

Extrapolation of these study findings to all of Bangladesh is not possible as it was conducted only among those KPs who were receiving STI services from DICs. Approximately half of the study participants were diagnosed with STIs previously (data not shown) using the syndromic approach and many had received antimicrobial therapy which could be the reason for the low recovery of *N. gonorrhoeae* strains. This is of relevance as the national syndromic guidelines for STI management in Bangladesh recommends treating gonorrhea and chlamydia with cefixime and azithromycin (6). However, with emerging resistance of *N. gonorrhoeae* to cefixime and ceftriaxone (8, 9), gonorrhea management guidelines are under scrutiny globally (10, 11). These current data from Bangladesh add to the global antimicrobial resistance data of *N. gonorrhoeae* and highlight the need to update the national guidelines for STI management in Bangladesh.

Funding information

This research protocol was funded by The Global Fund to Fight AIDS, Tuberculosis and Malaria (GFATM), grant number BAN-202-G13-H-00. The funders had no role in study design, data collection and interpretation, or the decision to submit the work for publication.

Acknowledgements

TA, RK, DA, MR, SIK and KHR designed the study and wrote the protocol. RK, MSA, MA and DA were in charge of staff training, field supervision and laboratory testing. TA, RK, MR, SIK, MSA, DA and KHM wrote the manuscript. All authors have contributed, read and approved the final manuscript.
We thank Masud Reza, Senior Manager, Infectious Diseases Division, for his help in data analysis.

Icddr,b acknowledges with gratitude the commitment of GFATM to its research efforts. Icddr,b is also grateful to the Governments of Bangladesh, Canada, Sweden and the UK for providing core/unrestricted support.

References


susceptibility of Neisseria gonorrhoeae isolated from Bangladesh during 1997-2006:


Table 1: Antimicrobial susceptibility to *N. gonorrhoeae* (n=21)

<table>
<thead>
<tr>
<th>Drugs</th>
<th>Sensitive % (n)</th>
<th>Intermediate % (n)</th>
<th>Resistant % (n)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cefixime</td>
<td>85.7 (18)</td>
<td>0 (0)</td>
<td>14.3 (3)</td>
</tr>
<tr>
<td>Azithromycin</td>
<td>90.5 (19)</td>
<td>0 (0)</td>
<td>9.5 (2)</td>
</tr>
<tr>
<td>Ceftriaxone</td>
<td>100 (21)</td>
<td>0 (0)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Ciprofloxacin</td>
<td>0 (0)</td>
<td>4.8 (1)</td>
<td>95.2 (20)</td>
</tr>
<tr>
<td>Doxycycline</td>
<td>4.8 (1)</td>
<td>4.8 (1)</td>
<td>90.5 (19)</td>
</tr>
<tr>
<td>Penicillin G</td>
<td>4.8 (1)</td>
<td>61.9 (13)</td>
<td>33.3 (7)</td>
</tr>
<tr>
<td>Spectinomycin</td>
<td>100 (21)</td>
<td>0 (0)</td>
<td>0 (0)</td>
</tr>
</tbody>
</table>