

Short Communication

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Resistance in *Neisseria gonorrhoeae*: A Cause of Concern?

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ABSTRACT

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Treatment failure or inability to attain bacteriological sterility in a patient with gonorrhoea has public health implications due to the potential for continued transmission and rapid emergence of antimicrobial resistance. Present study detects the antimicrobial susceptibility pattern of *N.gonorrhoeae* isolates from 200 patients attending STI clinic. Urethral/endocervical swabs were cultured on selective media and after confirmation the isolates were tested for antimicrobial susceptibility. Prevalence of gonorrhoea in present study was found in 4 % of which, 62.5% isolates were resistant to penicillin, 12.5% were PPNG and 25% isolates were TRNG, 100% QRNG and 37% had high level resistance to ciprofloxacin while, none had elevated MIC to ceftriaxone.

Introduction

Gonorrhoea, a disease well documented from ancient times, continues to defy man's attempt to control it. It is a successful pathogen with a remarkable journey over the years. It has been adept at developing resistance to several commonly used antimicrobials (Bala *et al.*, 2005).

The failure to cure a case of gonorrhoea has public health implications due to the potential for continued transmission and rapid emergence of antimicrobial resistance. Moreover, it also facilitates the spread of HIV. The present study was initiated to document the resistance pattern of *N.gonorrhoeae* isolates from patients

attending STI clinic at a large tertiary care hospital in East Delhi.

Experimental procedure

Two hundred consecutive patients, who attended the STI clinic of our hospital, were enrolled in the study. Urethral and endocervical swabs were collected from male and female patients respectively, with a suggestive history. Samples were subjected to direct examination by gram staining and culture isolation on chocolate agar (CA) with vancomycin, colistin, nystatin and trimethoprim supplements and incubated with 5-10% carbon dioxide for

24-48 hours at 37°C. A presumptive diagnosis of gonococcal urethritis was made on observing polymorphonuclear leucocytes with gram-negative intracellular diplococci. After confirming the isolates as *N.gonorrhoeae* by rapid carbohydrate utilization test, antimicrobial susceptibility testing (AST) of *N.gonorrhoeae* was done on CA by disc diffusion technique following the Antimicrobial Gonococcal Surveillance Programme (AGSP) method (based on CDS technique) using penicillin (0.5 IU), tetracycline (10 µg), ceftriaxone (0.5µg), spectinomycin (100 µg), ciprofloxacin (1µg), nalidixic acid (30 µg), azithromycin (15µg) and cefpodoxime (10 µg) (Oxoid, U.K). The annular radius of zone of inhibition was compared with interpretive standards and used to label isolates as sensitive / less sensitive / resistant. All the isolates were also tested for beta lactamase production by chromogenic cephalosporin disc method (Oxoid, U.K).

MIC of ceftriaxone was determined by E-strips containing 0.002-32µg/ml (AB Biodisks, Sweden) & based on MIC value isolates were labelled as ceftriaxone sensitive (MIC ≤ 0.03µg/ml) & less sensitive (MIC ≥ 0.06 µg/ml).

MIC of ciprofloxacin was determined by E-strips containing 0.002-32 µg/ml (Difco, USA) & based on MIC value isolates were labelled as ciprofloxacin sensitive (MIC ≤ 0.03µg/ml) and less sensitive (MIC between 0.06-0.5µg/ml) & resistant (MIC ≥1.0). WHO strains A to E obtained from WHO GASP SEAR Regional Reference Lab, New Delhi were used for quality control for disc diffusion and MIC testing.

Results and Discussion

In present study, all patients which were suggestive of gonorrhoea by gram stain isolated *N.gonorrhoeae* on culture.

Overall gonococcal urethritis was detected in 4% of our patients with a female predominance (M:F=3:5). These female patients were in the sexually active age group of 20-35 years. Most of the patients with gonorrhoea (75%) presented mainly with discharge which was thick and yellow in females & mucopurulent in male patients.

Penicillin resistance was observed in 62.5% of isolates of which 12.5% were Penicillin producing *N. gonorrhoeae* (PPNG). All PPNG isolates were found to be ciprofloxacin resistant. 25% of isolates were TRNG, but sensitive to other antibiotics. None of the isolates had elevated MIC to ceftriaxone. All isolates were resistant to ciprofloxacin and 37% among them had high level resistance to ciprofloxacin (MIC ≥8µg/ml). (Fig 1, Fig 2)

The number of patients with gonorrhoea at 4% in this study is much less when compared to an earlier study from the same location with a figure of 19.3% in the year 2010 (Choudhry *et al.*, 2010). Prevalence of gonorrhoea among STIs clinic attendees in different regions of India varies from 3-19 % (Sharma *et al.*, 2004). A higher rate of gonorrhoea in women is comparable to study from Mumbai (9.7%) and probably relates to their ignorance & stigma attached to the disease (Divekar *et al.*, 2000).

Our observation also underscores the emergence of penicillin resistance in *N.gonorrhoeae* isolates. Our data of PPNG at 12.5% is comparable to 8-66% reported from other parts of India and SEAR countries (Sunil *et al.*, 2006; Rahman *et al.*, 2002)). PPNG at 88% in North India was documented during 2011-2013 (Bharara *et al.*, 2015) and in WHO western pacific region their prevalence varies from 1% -90 % (Tapsall *et al.*, 2002). This brisk extension of PPNG is due to the dissemination of 4.4

MDa and 24.5 MDa plasmids associated with the Asian strains of *N.gonorrhoeae*.

Quinolone resistant *N.gonorrhoeae* (QRNG) is on the rise as evidenced by the present study (100%) and other reports from northern India (Sunil *et al.*, 2006; Bala *et al.*,2007; Bharara *et al.*,2015), thus, periodic monitoring is necessary. High QRNG is also documented from Bangladesh, Pakistan and

Bhutan (Ray *et al.*, 2005; Jabeen *et al.*, 2011). Elevated prevalence of QRNG probably indicates unregulated and misuse of these over-the-counter drug, and hence quinolone are no longer recommended for the treatment for gonorrhoea in India. Inappropriate use of this drug by malapropos health-care providers in South East Asia is a cause of great concern.

Fig.1 AST of *N.gonorrhoeae*.

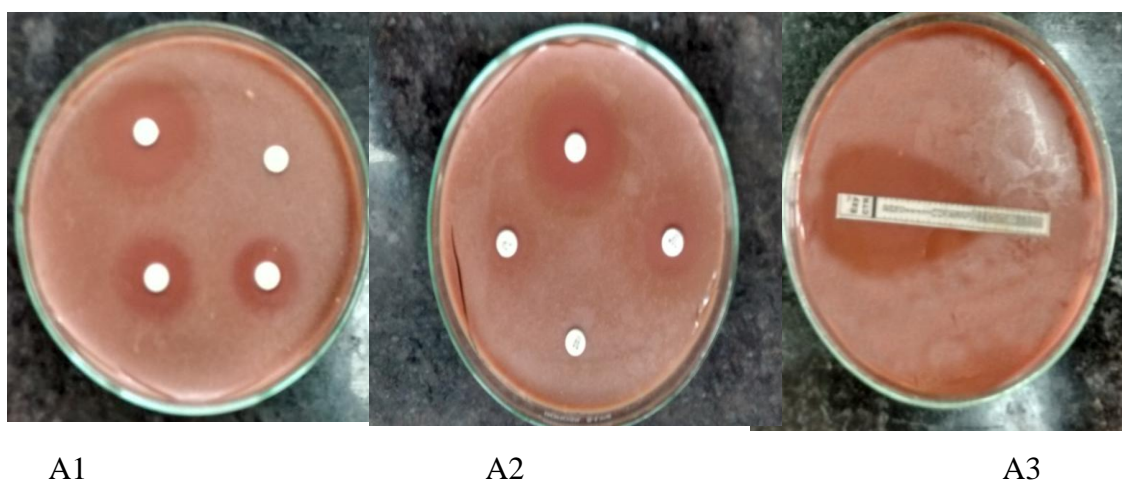
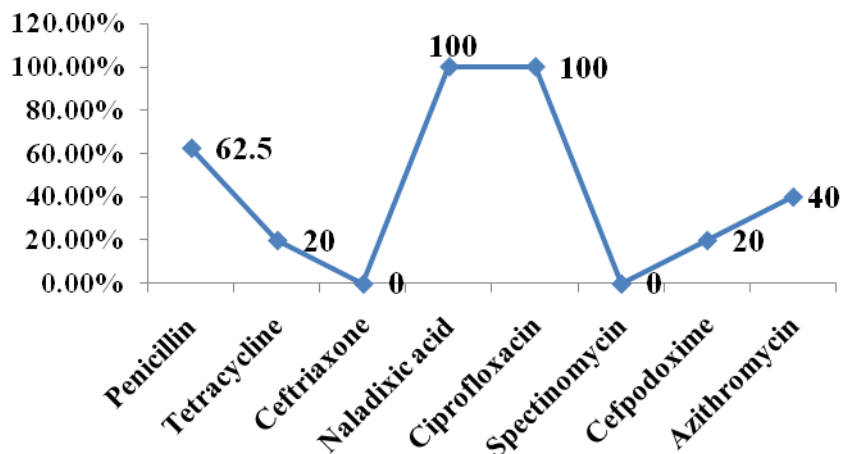


Fig.2 Antibiotic resistance pattern of *N.gonorrhoeae* strain.



TRNG has been documented to vary from 12 to 51% in North India (Bharara *et al.*, 2015; Sunil *et al.*, 2013). Our result (25%) is comparable with the above data. Reports

from South India document 33.8-45.6% TRNG (Ray *et al.*, 2005). Bangladesh and Pakistan have recorded higher TRNG (Ray *et al.*, 2005; Jabeen *et al.*, 2011).Location of

tet M gene on the transferable plasmid along with ongoing selective pressure due to the use of tetracycline in syndromic management of STIs as also to treat other clinical conditions may account for efficient transmission of resistance reflecting high TRNG.

Although decreased susceptibility to ceftriaxone (MIC ≥ 0.06 to up to $0.25 \mu\text{g/ml}$) has been reported from Delhi (Bala *et al.*, 2007; Bharara *et al.*, 2015), as early as 2001, Japan has reported resistance to extended spectrum cephalosporin even earlier (Muratani *et al.*, 2001). Similar reports followed from other countries (Tarsall *et al.*, 2006). Present study did not observe increased MIC to ceftriaxone. This however is still of concern since evolution of resistance has been shown to precede treatment failure complicating effective disease control in particular geographical regions.

In conclusion, clinical suspicion of gonorrhoea must be supplemented with laboratory isolation of the etiological agent for AST to guide appropriate treatment. It is recommended that the treatment of gonorrhoea should be with drugs which have efficacies that approach 100% & treatment with efficacies $< 95\%$ should never be used (Aggarwal *et al.*, 2002). In the light of high QRNG, TRNG & emergence of decreased susceptibility to extended spectrum cephalosporin, prudent use of drugs coupled with periodic monitoring of AST of consecutive GC isolates would help to preserve antibiotic effectiveness in the treatment of uncomplicated gonorrhoea and also prevent dissemination of drug resistant strains in the community. Continuous surveillance of antimicrobial resistance is thus crucial to tailor treatment schedules when the need arise and incorporate this activity as a necessary operating procedure.

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