

INCREASING PATTERN OF ANTIBIOTIC RESISTANCE IN NEISSERIA GONORRHOEAE

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ABSTRACT

Objectives: To explore the fact of increasing pattern of resistance to commonly used antibiotics by *Neisseria gonorrhoeae* detected simultaneously in gram-stained smears and cultures of urethral and / or prostatic secretions.

Design: Retrospective study to detect *N. gonorrhoeae* from the submitted urethral and / or prostatic secretions and their antibiogram.

Subjects: One hundred thirty three male patients of suspected gonorrhoea attending the Skin & V.D. outpatient's department of Rajshahi Medical College Hospital (RMCH), Bangladesh from January to November 2001.

Setting: The study was conducted at the Department of Microbiology of Rajshahi Medical College as a part of its diagnostic service delivery to the patients of RMCH.

Methods: Urethral and/or prostatic secretions were collected from the suspected cases of gonorrhoea. Gram-stained smears for microscopical detection of gram-negative diplococci and culture on Chocolate agar media were done for all samples. Antimicrobial susceptibility testing by standard disc diffusion method was performed using antibiotics commonly prescribed for the treatment of gonorrhoea.

Results: Significant number of cases was found to be positive for *N. gonorrhoeae* in both urethral and prostatic secretions. As tools for detecting *N. gonorrhoeae* both Microscopical examination and Culture were equally comparable. Bacterial isolates showed around 11.60% resistant cases against Ciprofloxacin and Gentamycin while Penicillin and Amoxycillin were found to be least efficacious drugs. Cephalexin, Doxycycline & Tetracycline were equivocal in sensitivity.

Conclusion: This study reinforces the microscopy of gram-stained smears as a good tool for rapid diagnosis of *N. gonorrhoeae*. It also explores the fact of increasing pattern of antibiotic resistance by *N. gonorrhoeae* to commonly prescribing drugs.

KEY WORDS: *N. gonorrhoeae*, Microscopy, Culture, Antimicrobial susceptibility testing.

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INTRODUCTION

Despite a substantial decrease in the incidence of gonorrhoea in Western countries in the recent past, a major burden of gonococcal

disease remains in developing and underdeveloped countries and also amongst the socially marginalized in the developed world¹. Extensive studies carried out in Africa, Latin America and Asia report that the incidence is highest in sub-Saharan Africa and lower in Latin America and Asia². Although the incidence is decreasing in many countries but with the increasing pattern of antibiotic resistance especially commonly used antibiotics, the successful treatment of gonorrhoea is becoming a problem day by day. Antimicrobial susceptibility patterns of *N. gonorrhoeae* vary in different geographical areas, specially in areas where ineffective treatment regimens are applied. This results in low plasma levels of the

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drug and a condition conducive to the selection of resistant mutant³.

The efficacy of various gonococcal treatment regimens is dependent upon the type, degree and prevalence of antibiotic resistance in the gonococcal population with the likely outcome of treatment closely paralleling the in-vitro susceptibility of the offending organisms⁴. However, because most treatment is provided before results of susceptibility tests on individual isolates can be obtained, therapeutic schedules are formulated on knowledge of the in-vitro sensitivity of prevalent gonococci. That is, the overall pattern of susceptibility of gonococci circulating in a region is the critical determinant of appropriate antibiotic therapy rather than individual strain susceptibility identified on a case-by-case basis⁵. Monitoring of antimicrobial resistance patterns in gonococci thus assists in the formulation and modification of standardized treatment regimens.

Penicillin and its synthetic derivatives have long been employed to combat gonococcal infections. But in the recent years, resistant strains of *N. gonorrhoeae* to Penicillin (PPNG) have limited its use in clinical practice. Newer antibiotics like Spectinomycin and newer generation Cephalosporins are more effective antimicrobials to treat gonorrhoea. Similarly, there is considerable number of resistant strains emerging against Quinolone antibiotics.

We have undertaken this study to detect *N. gonorrhoeae* by both microscopic examination of gram-stained smears and culture of urethral and prostatic secretions from male patients and to ascertain their antibiogram using commonly prescribed antibiotics to treat gonorrhoea.

PATIENTS AND METHODS

Urethral discharges and / or prostatic secretions from the suspected cases of gonorrhoea attending the Skin & VD out-patient department of Rajshahi Medical College Hospital were collected aseptically at the department of Microbiology, Rajshahi Medical College from January to November 2001.

All samples were inoculated onto chocolate

agar media and incubated aerobically at 37°C in an atmosphere of 5-10% CO₂ by candle extinction jar. Microscopic examination of gram-stained smears of each sample was done simultaneously to see gram-negative dipococci using Olympus CH-20 microscope. After a period of up to 48 hours incubation, growth of *N. gonorrhoeae* was identified by standard identification steps for *N. gonorrhoeae*^{6,7}. Growth of bacteria other than *N. gonorrhoeae* were excluded in this study.

All isolates were tested for antimicrobial susceptibility by disc diffusion method⁸ against Penicillin (10 units), Amoxycillin (25 µg), Tetracycline (30 µg), Doxycycline (30 µg), Cephalexin (30 µg), Gentamicin (10 µg) and Ciprofloxacin (10 µg).

RESULTS

A total of 133 samples were studied which included 85 (63.91%) urethral discharges and 48 (36.09%) prostatic secretions. Microscopic examination and culture of urethral secretions revealed 40 (47.05%) and 49 (57.65%) *N. gonorrhoeae* respectively. On the other hand, positivity of *N. gonorrhoeae* in prostatic secretions by microscopic examination and culture were 25 (57.08%) and 29 (60.42%) respectively (Table-I). It is evident from table-I that microscopic examination of all samples including both urethral and prostatic secretions revealed 65 (48.87%) positive cases of *N. gonorrhoeae* while culture of same number yielded 78 (58.65%) isolates of *N. gonorrhoeae*.

TABLE - I

Detection of *N. gonorrhoeae* in Urethral & Prostatic secretions in Microscopy and Culture

Specimens	Number studied		Number Positive	
Urethral secretion	Gram stain	Culture	Gram stain	Culture
	85 (63.91)	85 (63.91)	40 (47.05)	49 (57.65)
Prostatic secretion	48 (36.09)	48 (36.09)	25 (57.08)	29 (60.42)
Total	133 (100)	133 (100)	65 (48.87)	78 (58.65)

Figures in the parentheses indicate percentage

Table-II shows sensitivity and resistance patterns of the isolates against commonly used antibiotics for gonorrhoea. Ciprofloxacin and Gentamicin were found to be the most efficacious drugs in this study with only 11.54% and 11.67% resistant cases respectively. Doxycycline, Cephalexin and Tetracycline were effective in 60.26%, 53.85% and 46.15% cases respectively. Penicillin and Amoxycillin showed least efficacy against *N.gonorrhoeae* with effective only in 33.33% and 21.79% cases respectively.

Table-II
Antibiogram of isolated *N. gonorrhoeae*
(n # 78)

<i>Antimicrobials</i>	<i>Sensitive (%)</i>	<i>Resistance (%)</i>
Ciprofloxacin	69 (88.46)	09 (11.54)
Gentamicin	65 (88.33)	13 (11.67)
Cephalexin	42 (53.85)	36 (46.15)
Doxycycline	47 (60.26)	31 (39.74)
Tetracycline	36 (46.15)	42 (53.85)
Amoxycillin	17 (21.79)	61 (78.21)
Penicillin	26 (33.33)	52 (66.67)

DISCUSSION

Neisseria gonorrhoeae the causative agent of gonorrhoea is a particularly well-adapted pathogen that has continued to evolve mechanisms to evade treatment with antimicrobial agents. In recent years a trend towards increasing resistance to both traditional and more recently introduced therapeutic agents has been observed amongst *Neisseria gonorrhoeae*⁹. The choice of antibiotic for use in the first line treatment of gonorrhoea should be made with the knowledge of the susceptibility of *N. gonorrhoeae* to be encountered. High-level resistance to penicillin and tetracycline in *N. gonorrhoeae* is plasmid mediated and a major therapeutic problem^{10,11}. Penicillinases producing *N. gonorrhoeae* first described in 1970 have now spread worldwide and tetracycline resistant *N. gonorrhoeae*, described in 1985, are becoming increasingly prevalent¹².

We have examined 133 samples, which

included both urethral discharges (63.91%) and prostatic secretions (36.09%) in this study. Gram-stained smears of each of the samples were examined under microscope, which revealed 47.05% and 57.08% positivity in urethral and prostatic smears respectively. On the other hand, culture of the samples yielded 57.65% and 60.42% of *N. gonorrhoeae* in urethral and prostatic secretions respectively. It is quite evident and also reinforces that microscopic examination of gram-stained smears is a very good tool for the rapid diagnosis of gonococcal infections. From the results it is revealed that detection of *N. gonorrhoeae* in microscopic examination is quite comparable with that of culture. Hence, situations where facilities for bacteriological cultures are not available good quality microscopy can help in diagnosing *N. gonorrhoeae* in the suspected cases. This is true for countries like Bangladesh because we have very limited centres where bacteriological culture facilities are available. Regarding rate of isolation, the present study is in accordance with our previous report from this department¹³.

In case of antimicrobial susceptibility of the isolates, we have observed that Ciprofloxacin and Gentamicin were effective drugs with only 11.54% & 11.67% resistance respectively. Ciprofloxacin is a fluoroquinolone and is highly active against *N. gonorrhoeae*. This antibiotic has only been in routine use for the treatment of gonorrhoea for about a decade¹⁴. Particular interest is centered on emergence of gonococcal resistance to this group of until-now useful oral antibiotics. In the recent years increasing number of Ciprofloxacin resistant *N. gonorrhoeae* are being reported from different centres. In the WHO report on Western Pacific Gonococcal Antimicrobial Surveillance Programme 1995, China, Hong Kong, Japan, and Vietnam had 15.5%, 7.7%, 29.4% and 5.5% Ciprofloxacin resistant cases respectively. These findings are quite similar with the present study. Interest remains in the extent and type of resistance to the Penicillins, although the clinical usefulness of this group of antibiotics has decreased significantly over a number of

years. High levels of Penicillin resistance were recorded in Vietnam (98%), Korea (90%), China (84%) and Malaysia (80%). We also observed significant number of cases (about 70%) resistant to Penicillin in this setting. Another important antibiotic commonly used in gonococcal treatment is Tetracycline and the resistant pattern observed against this drug in this study (54%) is quite in accordance with nearby countries like Malaysia (58.5%), Singapore (63.8%) and Vietnam (42.3%)¹⁵.

Finally we would like to conclude by correlating the global problem of HIV and gonorrhoea. It is now acknowledged that gonorrhoea is a potent cofactor in the transmission of the Human Immunodeficiency Virus (HIV)¹⁶. The converse of this situation is that better Sexually Transmitted Disease (STD) treatment and, through it, a reduction in the prevalence of STDs, reduces HIV transmission¹⁷. There are thus clearer and more cogent reasons than ever before to ensure that gonococcal disease is properly treated when it cannot be otherwise prevented. Continuing surveillance of gonococcal sensitivity patterns can not only alert us to changes in resistance as they emerge, but also allow timely, appropriate and cost-effective implementation of decisions on antibiotic therapy.

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