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ANTIMICROBIAL SENSITIVITY OF *NEISSERIA GONORRHOEA* IN GONDAR, ETHIOPIA

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ABSTRACT

**Objectives:** To determine the antimicrobial susceptibility pattern of *Neisseria gonorrhoeae* and to obtain epidemiological information on resistance of *Neisseria gonorrhoeae* in Gondar town.

**Design:** A cross sectional study.

**Setting:** Gondar Health Centre.

**Subjects:** One hundred and seventy eight male patients presented with urethral discharge and who volunteered to participate in the study were included.

**Results:** A total of 142 strains of *N. gonorrhoeae* were isolated from 168 cultures received. The sensitivity of gonococcal isolates ranges from 98.6% to chloramphenicol to 7.7% to cotrimoxazole. Multiple drug resistance was reported in 87.5% of isolates and only four isolates were sensitive to all antibiotics. One strain of *N. gonorrhoeae* was resistant to as many as eight antibiotics (tetracycline, penicillin, ampicillin, kanamicin, methicilin, carbenicillin, cotrimoxazole and ceftriaxone). More than eighty five per cent of the isolated strains were penicillinase-producing *Neisseria gonorrhoeae* (PPNG).

**Conclusion:** Gonococcal resistance is a significant public health problem in Gondar region and the drugs recommended for treatment of gonococcal cases by the national sexually transmitted diseases (STDs) control programme need to be revised.

INTRODUCTION

The introduction of penicillin for the treatment of gonorrhoea was thought to have a considerable impact to the elimination or at least to its control. Even though the fall in the number of gonococcal infection cases following treatment with penicillin was initially marked, subsequent chromosomal mutation led to progressive increase in resistance(1). The percentage of strains with chromosomally determined resistance has increased over the years requiring the administration of increasing dose of penicillin to achieve satisfactory response(2).

The problem of antibiotic resistance of *N. gonorrhoeae* has been aggravated by the emergence of penicillinase-producing *Neisseria gonorrhoeae* strains. The situation is worsening in developing countries where penicillin resistant strains of *N. gonorrhoeae* predominate. Thus, resistant strains should be continuously evaluated for better and effective management of cases.

Gonorrhoea is one of the most widely prevalent STDs in Ethiopia accounting for 60% of all STDs. Since the

launching of the STD control programme in 1989, priority has been given to carry out studies which could provide us with reliable evidence to suggest the appropriate antibiotic for effective treatment of gonorrhoea.

In Ethiopia the first cases of penicillin resistant *N. gonorrhoeae* were reported in 1969. The existing epidemiological data on susceptibility of *N. gonorrhoeae* isolates demonstrate an increase in resistance (50-80%) to penicillin since 1973(3-6). Presence of PPNG strains was also further demonstrated to be 31%, 49% and 73% in 1983, 1987 and 1990, respectively(8,9).

In 1990 operational research conducted in Addis Ababa, Ethiopia, among 72 females with multiple sexual partners revealed that the prevalence of PPNG strains was 73%, all of which were resistant to penicillin, 96% ampicillin and 81% to cotrimoxazole. Nineteen per cent of non-penicillinase producing *N. gonorrhoeae* were resistant to penicillin, 38.1% to kanamicin, 66.6% to cotrimoxazole and 66.7% to ampicillin. None of the isolates were resistant to tetracycline(8).

The specific objectives were: to determine the proportion of gonococcal urethritis; to determine the proportion of PPNG strains; to assess the sensitivity of *N. gonorrhoeae* isolates for eleven anti-microbial agents and; to obtain epidemiological information on resistance of *N. gonorrhoeae*.

## MATERIALS AND METHODS

**Design and participants:** This cross sectional study was conducted in Gondar Health Centre. Male patients, coming for the first time to the health unit with symptoms of urethral discharge and who consented to participate in the study, had not been referred from another health unit for this episode were selected.

One hundred and seventy eight male patients with urethral discharge participated in the study, but data were analysed for 168 patients. The rest were omitted in analysis either due to incomplete information or problems in specimen collection.

**General procedure:** For 178 patients with urethral discharge, informed consent was sought. Data were collected using a questionnaire consisting of information on socio-demographic variables, symptoms and signs suggestive of gonococcal urethritis and self-treatment in the last two weeks. Following a short interview, a health care provider did a physical examination and a specimen taken by passing a sterile cotton swab in the distal urethra.

**Laboratory procedure:** The specimen was transported in Amies transport medium to Gondar College of Medical Sciences laboratory for further processing. Upon arrival at the laboratory, samples were inoculated onto modified Thayer-Martin agar plates. All the plates were incubated immediately at 35°C - 36°C in a humidified atmosphere containing 3-5% CO<sub>2</sub> for at least 48 hours *Neisseria gonorrhoeae* were identified by Gram stain, colony morphology, oxidase test and carbohydrate utilisation test. All the isolated strains were also tested for beta lactamase production using a chromogenic cephalosporine reagent. The isolated strains were stored at -20°C until the performance of antibiotic sensitivity testing following the disk diffusion method. The antibiotic panel included penicillin, ampicillin, methicillin, carbencillin, erythromycin, tetracycline, chloramphenicol, cotrimoxazole, gentamicin, kanamycin and ceftriaxone. The level of sensitivity was determined by measuring the diameter of inhibition zone for the specific antibiotics.

**Data analysis:** Information collected from interview and laboratory results were entered and analysed using EPI-6.0 statistical software package. Statistical analysis was tested using  $\chi^2$  test.

## RESULTS

The mean age of clients was 28±8 years. More than 95% of the participants were below the age of 40 years while 57.2% were between the age of 20 and 30 years (Table 1). The mean and median duration of complaint were 27 days and 14 days, respectively (Table 2).

The major complaints of the patients were urethral discharge (63.1% had spontaneous discharge and 36.9% had discharge on milking of the urethra), pain during urination and itching (Table 3).

**Table 1**

*Distribution of age of male patients with urethral discharge*

Age (years)	n=268	%
<15	1	0.6
15-19	12	4.5
20-24	49	18.3
25-29	47	17.5
30-34	28	10.5
35-44	25	15.1
45-54	5	3.0
55-64	2	1.2

**Table 2**

*Duration of complaints of male patients with urethral discharge*

Duration of complaint (day)	n=268	%
1-7	57	34.1
8-14	30	18.6
15-28	29	17.4
29-59	38	21.6
60+	14	8.4

**Table 3**

*List of complaints presented by patients with urethral discharge*

Complaint	n=142	%
Spontaneous discharge	90	63.1
Discharge on milking	52	36.9
Dysuria	150	89.9
Itching	51	30.9

**Table 4**

*Self-treatment history of patients with urethral discharge*

Type of antibiotic	Mode of treatment				Total
	Single		In-combination		
	No.	%	No.	%	
Tetracycline	22	50.0	22	50.0	44
Cotrimoxazole	20	46.0	22	54.0	42
Ampicillin	10	41.5	14	58.5	24
Penicillin	6	30.0	14	70.0	20
Rifampicin	2	50.0	2	50.0	4
Spectinomycin	1	25.0	3	75.0	4
Metronidazole	1	33.3	2	66.7	3
Chloramphenicol	1	100	-	-	1

Fifty six point five percent of patients had a history of self-treatment for the current episode in the last two weeks and the commonly used antibiotics were tetracycline, cotrimoxazole, ampicillin and penicillin. One third had history of multiple drug treatment, the commonest combination being ampicillin with tetracycline. Only 53.7% had claimed taking a full course of antibiotics for the illness (Table 5). Direct microscopy of the discharges revealed that 72.3% of the smears had  $\geq 5$  polymorphonuclear cells indicating acute inflammatory response in the urethra. 70.1% had intracellular diplococci on Gram stain.

Table 5

Sensitivity test results of antimicrobial agents for *N. gonorrhoea* isolates

Antibiotic	Sensitive strains (n)	%
Chloramphenicol	140	98.6
Erythromycin	137	96.5
Ceftriaxone	136	95.8
Gentamicin	122	85.9
Kanamycin	119	83.8
Tetracycline	100	70.4
Carbenicillin	92	64.8
Methicillin	29	20.4
Ampicillin	28	19.7
Penicillin	21	14.8
Cotrimoxazole	11	7.7

In one hundred and forty two (84.5%) of the specimen, diagnosis of gonococcal infection was confirmed using the modified Thayer-Martin media. Eighty five percent of the isolates were PPNG positive, of which 34.2%, 95.1% and 96.8% were resistant to tetracycline, cotrimoxazole and penicillin, respectively.

All isolates were tested for susceptibility and it was found that 140 (98.6%), 137 (96.5%) and 136 (95.8%) of strains were sensitive to chloramphenicol, erythromycin and ceftriaxone, respectively. The highest resistance found was to cotrimoxazole in 131 (92.3%), followed by penicillin in 123 (86.6%), ampicillin in 114 (80.3%) and methicillin in 113 (79.6%) (Table 5). Multiple drug resistance was found in 87.5% of the isolates and only four isolates were sensitive to all antibiotics. One strain of *N. gonorrhoeae* was resistant to as many as eight antibiotics (tetracycline, penicillin, ampicillin, kanamycin, methicillin, carbenicillin, cotrimoxazole and ceftriaxone.)

PPNG strains were found to be associated with resistance not only to penicillin and its derivatives but also to tetracycline and cotrimoxazole ( $p < 0.05$ ) but not to erythromycin. Resistance to penicillin and tetracycline were associated with prior self-treatment with the same drugs. The duration of complaints was not associated with resistance to the antibiotics.

## DISCUSSION

The results indicate that most of the cases of gonococcal urethritis were from sexually active adolescents and young adults. This is in agreement with results obtained from other studies(14).

The mean duration of complaints was 27.3 days, which is quite long for gonococcal urethritis and this may be due to higher rates of self-treatment with inappropriate regimen. The proportion of gonococcal urethritis was 84.5%. This is higher compared to other studies in which only 29% and 35% of urethritis were due to *N. gonorrhoeae*(10,14). History of self-treatment was 56.5%. This is higher than the results reported from a study done on female sex workers in Addis Ababa in which only 20% had a history of self-treatment spreading over a one week period. This may be due to differences in the two populations.

The commonly used drugs for self-treatment were tetracycline and cotrimoxazole; the drugs which are

recommended by the national STDs and AIDS control for gonococcal infection in Ethiopia(12). The use of multiple drugs mainly purchased from local drug shops and under-treatment or non-cure treatment were the major problems which may have a significant impact on the sensitivity pattern of these antimicrobials(7,8,14).

The proportion of PPNG strains was 86.5%, which is higher compared to other studies that show ranges from 25% - 80%(3,4,5,7,13,14). The sensitivity of commonly used antimicrobials for the treatment of gonorrhoea is lower than that reported from previous studies and especially the sensitivity of tetracycline and cotrimoxazole which was reported to be as high as 100% and 66.6%, respectively. The two drugs seem to have little effect in the treatment of gonococcal urethritis(5,7).

Based on the above findings we propose the following recommendations: (i) the use of antibiotics should be controlled because of the emerging multiple drug resistance to gonococci.; (ii) recommended antibiotics like cotrimoxazole should not be prescribed for gonococcal urethritis unless sensitivity testing is done and isolates confirmed to be sensitive. The introduction of a new regimen should be considered in the syndromic management of urethral discharge since the presently recommended drugs like cotrimoxazole and tetracycline are less effective in an *in vitro* test for gonococcal urethritis.

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