

## ORIGINAL RESEARCH

## GONORRHOEA IN MEN: DIAGNOSTIC ASPECTS AND CHANGING ANTIBIOTIC SUSCEPTIBILITY PATTERN

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## ABSTRACT

**Background:** Gonorrhoea since the ancient times is causing significant morbidity. Though a number of methods are available for diagnosis in men, culture still remains the gold standard. Gonococci are delicate and fastidious bacteria but its remarkable ability to develop resistance to a variety of antibiotics makes it a major threat to public health.

**Objectives:** To detect the incidence in symptomatic men and in vitro antimicrobial susceptibility pattern of the gonococcal isolates.

**Materials & Methods:** - 100 urethral swabs from men with urethritis were screened for presence of gonococci by gram stain and culture on Chocolate Agar and Modified Thayer-Martin medium. The isolated gonococci were screened for Penicillinase production and susceptibility to antibiotics was subsequently carried out by standard disc diffusion method.

**Results:** - Gonorrhoea was detected in 56 of the urethral swabs giving a incidence of 56%. The difference of detection in gram stain and culture was insignificant ( $P > 0.05$ ). Of all the isolated gonococci considerable resistance was seen to ciprofloxacin(46.4%), tetracycline(23.2%) and Penicillin(17%) with Incidence of PPNG being 12.5%. All strains were uniformly sensitive to Spectinomycin and Cephalosporins.

**Conclusions:** - *Neisseria gonorrhoeae* is main etiological agent in urethritis in sexually active men and culture though time consuming, costly and demands expertise is still better method for diagnosis as gives high isolation rate and observe changing patterns in antibiotic susceptibility to commonly used antimicrobials.

**Keywords:** Gonorrhoea, Men, Antibiotic susceptibility

## INTRODUCTION

Gonorrhoea is one of the oldest known bacterial diseases that was recognized as sexually transmitted infection by 13<sup>th</sup> century but still causes significant morbidity among sexually active individuals<sup>1</sup>. Global estimates of disease are difficult to obtain but WHO suggests that worldwide, 62 million new cases occur annually. The greatest burden of disease falls upon less developed countries so the highest incidence and prevalence is found in Africa and South-East Asia. In India, the prevalence rate of gonorrhoea is 3-19%<sup>2</sup>. Gonorrhoea caused by *Neisseria gonorrhoeae*, is diagnosed presumptively by the presence of intracellular and extracellular Gram negative cocci on a Gram stain. Culture for the causative organism is considered necessary, however, as it dies rapidly if exposed to desiccating or oxidising conditions, so isolation of gonococci requires good specimen collection and bedside inoculation or suitable transport, a moist carbon dioxide enriched atmosphere and enriched and or selective medium<sup>3,4,5</sup>. For these reasons diagnosis by

culture was regarded as difficult and uncertain, but many decades ago the problems were overcome, and culture became the method of first choice for diagnosis, and remains the "gold standard" against which other methods are measured. However, culture is by no means the only method available for diagnosis of gonorrhoea.<sup>3,4,5</sup>

Alternative methods have been evaluated exclusively for the detection of gonococci in clinical specimen such as ELISA, immunofluorescence, DNA probes, genetic transformation, polymerase chain reaction (PCR). Though rapid, sensitive and specific, PCR has several limitations; it needs costly equipment and reagents, experienced technician, and the organism cannot be isolated in this method for further investigation.<sup>5,6</sup> On the other hand, culture, though more time consuming, needs to maintain viable organism till culture is done and having less sensitivity in some samples, is the method of choice for identification of gonococci, particularly in developing countries because is cost effective, high specificity and very important for testing

the antibiotic sensitivity pattern that is another key factor in successful treatment and control of disease<sup>3,5</sup>. Because of continuing drift towards decreased antibiotic sensitivity of *Neisseria gonorrhoeae*, effective treatment of gonorrhoea is hampered. Emergence of gonococci with plasmid mediated and chromosomally mediated resistance to penicillin and tetracycline resulted in use of quinolones for the treatment of gonorrhoea. But Quinolone Resistant *N. gonorrhoeae* (QRNG) resulted in the use of expanded spectrum Cephalosporins as the first line of treatment for uncomplicated gonorrhoea. Because of the emergence of resistance to different antibiotics, the in vitro estimation of antimicrobial sensitivity becomes necessary.<sup>7</sup> There has been little published work on gonococcal infection in men since before the 2nd World War and much that is written reflects received information, passed down from previous authorities.<sup>8</sup>

So this study was carried out in symptomatic male patients to know the incidence of gonococci in urethritis and evaluation of gram stain and culture methods as well as role of enriched media and selective media in diagnosis of gonorrhoea and study antibiotic susceptibility pattern of gonococci.

**METHODS AND MATERIAL**

Male patients with complaint of urethral discharge were examined after informed consent. Those suspected of having gonorrhoea, discharge was collected under sterile conditions and smears were prepared for Gram staining and culture performed bed side on enriched media and selective media. For this purpose two samples were taken one for culture and second for smear preparation.

**Table 1: Incidence of gonorrhoea and Evaluation of Chocolate agar (CA) and Modified Thayer Martin (MTM) medium in isolation of gonococci**

Authors	Total	Gonococcal isolates (%)	No. of isolations on specific media		
			MTM + CA	MTM only	CA only
Present study	100	56(56%)	53	03	00
Jacob et al <sup>9</sup>	375	169(45%)	158	10	01
Bonin et al <sup>10</sup>	6236	868(13.9%)	839	16	13

Majority of patients (78.6%) with gonorrhoea were between 15 to 29 yrs of age and 94.6% gave history of unprotected sexual exposure to CSWs while 5.4% were homosexuals. Diagnosis of gonorrhoea was established by Gram stain in 53% and by culture in 56% of the patients but the difference of positivity is not statistically significant (P>0.05) (Table 2).

Gonococci were isolated on both MTM and CA in 53 cases, on MTM only in 3 and no isolation on CA only. So all the isolates grew on MTM and only 3 were not isolated on CA. Though the rate of isolation is higher on MTM in comparison to CA, the difference is not statistically significant (P>0.05) (Table 1). All the isolates were susceptible to Spectinomycin, Cefuroxime and Ceftriaxone. While 23.2% and 46.6% were resistant to

1. A sterile, calcium alginate tipped swab was used for collection of discharge or sterile bacteriological loop was passed 3-4 cm into the urethra. One swab was used for smear preparation for Gram-staining and microscopical examination. Gram-stained smears of urethral exudate were examined under x 1000 magnification oil immersion for the presence of polymorphonuclear cells and Gram-negative diplococci. The results of the smears were considered positive if typical Gram-negative diplococci were seen, whether located intracellularly or extracellularly.

2. And the second swab was streaked directly on to an enriched medium, Chocolate Agar(CA) and selective medium, Modified Thayer-Martin media(MTM) having Vancomycin, Colistin, Nystatin and Trimethoprim as selective agents and incubated for 48 hours in moist environment at 35-36°C in 5-10% carbon dioxide. No cultures for viruses or chlamydiae were carried out. A presumptive identification of isolates of *Neisseria gonorrhoeae* was based on characteristic colonial morphology, positive oxidase test, and the presence of Gram-negative diplococci. Isolates were further identified as *N. gonorrhoeae* by typical sugar utilization tests. All the isolated gonococci were screened for production of Penicillinase by acidometric method and antibiotic sensitivity testing performed by disc diffusion method against Penicillin, Tetracycline, Ciprofloxacin, Spectinomycin, Cefuroxime and Ceftriaxone.

**RESULTS**

In the present study, gonococci were the etiological agent in 56(56%) of the 100 symptomatic men that presented with urethritis (Table 1).

tetracycline and ciprofloxacin respectively. Resistance to penicillin was observed in 10 (17.8%) of the isolates of which Penicillinase producing *Neisseria gonorrhoeae* (PPNG) were seen in 7(12.5%) of the isolates (Table 3).

**Table 2: Evaluation of smear in comparison with culture in diagnosis of gonorrhoea**

Authors	Positive by smear (%)	Positive by culture
Present study (n =100)	53(94.6)	56
Manis et al <sup>11</sup> (n=295)	98(95.1)	103

**Table 3: Antibiotic resistance pattern of gonococci**

study	Penicillin (%)		Tetracycline (%)	Ciprofloxacin (%)	Spectinomycin (%)	Cefuroxime (%)	Ceftriaxone (%)
	PPNG	Non PPNG					
Present study (n=56)	7 (12.5)	3 (5.3)	13(23.2)	26(46.4)	00	00	00
Lesmana et al (n=122)	77 (63.1)	6 (4.9)	119(97.5)	---	00	00	00
Berron et al (n=400)	150 (37.5)	16 (4)	129(32.2)	26(6.5)	00	----	00

## DISCUSSION

Among the symptomatic males gonococcal urethritis is the predominant (56%). Similar results are reported by Jacob et al<sup>9</sup> (P>0.05) but the incidence is significantly different with that of Bonin et al<sup>10</sup> (P<0.01) (Table 1). This difference is because in present study only cases of symptomatic urethritis have been included while Bonin et al included all male patients undergoing urethral culture whether for diagnosis, screening or test of cure. On comparison with study of Manis et al<sup>11</sup>, the rate of positivity of smear in diagnosis of gonorrhoea is not statistically significant (P>0.05) (Table 2). Similar results were reported by Sherrard et al<sup>8</sup> 94% positivity of smear in symptomatic men. These results further confirm that Microscopy of a gram-stained urethral sample is a highly sensitive examination in diagnosis of gonorrhoea when compared to culture in symptomatic men, although its sensitivity is much reduced in asymptomatic men, even when most of these are presenting as known contacts of gonorrhoea, and the index of suspicion of the microscopist is high<sup>8</sup>. On comparing result of present study for isolation on CA and MTM with that of Jacob et al<sup>9</sup> and Bonin et al<sup>10</sup>, it was observed that the difference was not statistically significant (P>0.05, CI 95%). However, in both the studies some isolates (1 in Jacob et al and 13 in Bonin et al) were isolated only on CA that may be because some strains of gonococci are susceptible to Vancomycin that inhibits growth on MTM which justifies use of Lincomycin in selective media instead of Vancomycin. and use of both enriched media and selective media in isolation of gonococci<sup>3,5,12</sup>. Antibiotic susceptibility pattern of gonococci in different geographical areas shows a lot of variation and very high resistance to commonly used antibiotics suggesting continuous monitoring of the susceptibility pattern to avoid over exposure to resistant antimicrobials.<sup>13,14,15</sup> Lesmana et al<sup>13</sup>, Berron et al<sup>14</sup> and Bhalla et al<sup>7,15</sup> in different studies in different geographical areas at different times also observed 0% resistance to Spectinomycin and Cephalosporins. However, in all the forementioned studies the resistance to Tetracycline was 64%<sup>7</sup>, 98%<sup>13</sup> and 32%<sup>14</sup>, Ciprofloxacin was 6.5%<sup>14</sup> and 75%<sup>15</sup> and to Penicillin was 12%<sup>7</sup>, 68%<sup>13</sup> and 41%<sup>14</sup>. This shows a lot of variation in resistance pattern in different geographical areas at same time and from time to time in the same region.<sup>7,13,14,15</sup>

## CONCLUSION

From the present study, we conclude that *Neisseria gonorrhoeae* is the predominant cause (56%) of urethritis in men. Majority of the patients were in age group of

20-29years of age and gave history of unprotected, multiple, heterosexual exposure to CSWs (94%). As for establishing diagnosis, though Gram stain is rapid, cost effective, highly sensitive and specific in symptomatic men we still recommend use of culture along with Gram stain. Culture though time consuming, costly, requires special set up and technical expertise and viable organism for isolation will help in diagnosis in missed out cases and perform Antibiotic sensitivity testing considering changing patterns in the sensitivity profile of organism<sup>4</sup>. As for choice of culture media whether enriched (CA) or selective (MTM), we recommend both, because MTM have higher isolation rate but some strains of gonococci are sensitive to Vancomycin and are inhibited on MTM are isolated only on CA. Due to high prevalence PPNG and resistance in gonococci to Penicillin, Ciprofloxacin and Tetracycline it is mandatory to perform antibiotic sensitivity testing and observe the changing pattern in antibiotic susceptibility pattern. However, because no resistance is observed to Cephalosporins these are the drugs of choice for management of Gonorrhoea.

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