

A clinico-etiological study of urethritis in men attending sexually transmitted disease clinic at a tertiary hospital

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Abstract

Introduction: Urethritis is an important sexually transmitted infection in the present day. Causative agents are many for urethritis, ranging from bacteria, virus, to protozoa. **Aim:** The aim was to study the various etiological agents and clinical presentation of men with urethritis. **Materials and Methods:** This was a cross-sectional study conducted at a tertiary care center in Bengaluru. After taking written informed consent, 100 men with symptoms of urethritis were enrolled in the study. Their demographic details, presenting symptoms, and examination findings were documented using a questionnaire and a pro forma. Results were tabulated and analyzed using mean. **Results:** Nearly 68% had urethral discharge with dysuria as the presenting symptom. Nearly 27% had only dysuria without discharge as the main complaint. Almost 15% had coexistent genital ulcer disease. Human immunodeficiency virus infection was present in 10% in the population studied. The most prevalent organism isolated was *Neisseria gonorrhoeae* (45%). Chlamydia trachomatis was isolated in 13%. *Trichomonas vaginalis* was isolated in two patients. **Conclusion:** Our study highlights the high prevalence of gonorrhoea in India when nongonococcal urethritis is the forerunner in the Western world. In addition, *T. vaginalis* as a cause of urethritis has to be considered in our setup.

Key words: Chlamydia trachomatis, Neisseria gonorrhoea, polymerase chain reaction, urethritis

INTRODUCTION

Urethritis is defined as inflammation of urethra. It is mostly a sexually transmitted disease (STD).

Urethritis manifested by urethral discharge, dysuria, or itching at the tip of urethra is the response of the urethra to inflammation of any etiology.^[1] The characteristic finding is urethral discharge, and pathognomonic confirmatory laboratory finding is

an increase in polymorphonuclear leukocytes on Gram-staining of urethral smear.

In the present day, STDs are on the rise. The reasons are many; urbanization, migration to the cities for job, late marriages, and sexual liberation being a few of them. A plethora of STDs is present and the list continues to grow with the discovery of newer STDs. Some of the venereal diseases have grand-old

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10.4103/ijstd.IJSTD_98_15

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How to cite this article: Nayak AK, Anoop TV, Sacchidanand S. A clinico-etiological study of urethritis in men attending sexually transmitted disease clinic at a tertiary hospital. Indian J Sex Transm Dis 2017;38:136-41.

history such as syphilis and gonorrhea whereas STDs of the modern era are human immunodeficiency virus (HIV) infection, herpes genitalis, hepatitis B, and nongonococcal urethritis.

The present study aims to study various etiological agents and clinical presentation of urethritis in men.

MATERIALS AND METHODS

The present study was conducted at the Department of Skin and STD in a tertiary care center at Bengaluru. One hundred sexually active males with the complaints of urethral discharge, dysuria, and symptoms suggestive of urethritis who visited our outpatient department, consecutively, were taken for the study over a period of 20 months. Women were excluded from the study.

After obtaining informed consent, patients were enquired about their address, age, marital status, education, socioeconomic status, occupation, and whether they had migrated or not. Presenting complaints were noted, mainly emphasizing on urethral discharge and dysuria. A brief questionnaire regarding sexual behavior of the patients was noted. A complete general, cutaneous, and systemic examination was done. Genital examination was carried out to look for the presence of any urethral discharge (spontaneously or on milking urethra), for the presence of genital ulcer, inguinal lymphadenopathy, or any other co-existing STD.

Three urethral swabs were taken:

1. One swab was taken and inoculated on to modified Thayer Martin medium. It was kept in candle extinction jar and sent to the microbiology department for incubation. Results were analyzed by the microbiologist
2. The second swab was put in an aliquot and kept in freezer to be sent for polymerase chain reaction (PCR) analysis
3. The third urethral swab was smeared for Gram-staining and wet mount. Gram-stained smear was examined for the presence of Gram-negative diplococci. Wet mount preparation was examined for motile organisms.

Fifteen milliliters of urine was collected after the swab collection. Urine was collected at a minimum of 1–1½ hours after the previous voiding. Leukocyte esterase dehydrogenase (LED) dipstick analysis was done by dipping the dipstick into the urine and kept for 2 min and it was looked for color change. It was graded according to the color change into negative, traces, or positives.

Exactly 0.5 ml of urine was put in an aliquot and frozen (for PCR analysis).

Ten milliliters of urine was centrifuged, the sediment was used to inoculate into the Inpouch TV medium for *Trichomonas vaginalis* culture. The Inpouch TV was sent to microbiology department for incubation. Culture was looked for *T. vaginalis* on 3rd and 7th days by the microbiologist. Five milliliters of venous blood was collected. Sera was analyzed for ELISA HIV (1 and 2) and venereal disease research laboratory (VDRL).

The urethral swab and urine in aliquot (frozen) were sent for PCR analysis. Both swab and urine were analyzed by PCR (Roche Company, USA) for *Chlamydia trachomatis* and *Neisseria gonorrhoeae*. Both swabs and urine were analyzed for *Mycoplasma genitalium* by PCR. (in-house PCR).

RESULTS

A total of 100 patients with symptoms of urethritis were studied.

Patients' age ranged from 16 years to 50 years. The youngest patient included in the study was 16 years old. The mean age of acquiring urethral infection was 33 years. Most of the patients were in the age group of 21–25 years.

Patients who could sign and were able to read were considered as literates. Nearly 56% of the patients in the study were literates with an ability to sign. Almost 75% of the study population did not use condoms. The remaining 24% were using condom regularly. One patient denied sexual exposure. Nearly 8% of the patients had anal sex at some point in their lifetime.

Age at which patients had a sexual exposure for the first time was noted. Most of them had the first exposure at or around 20 years (20–24 years) [Table 1]. One patient denied sexual exposure. In addition, it was found that 55% of these patients had visited commercial sex workers at some point in their lifetime. About 84 patients had two or more sexual partners. Almost 48% of the

Table 1: Age at the first intercourse

Age	Number of patients
10-14 years	2
15-19 years	40
20-24 years	46
25-29 years	9
30-34 years	2

study patients were migrants. Nearly 30% belonged to the laborer group (coolie, unskilled).

Nearly 91% of the study population was heterosexuals, whereas 8% were bisexuals. One patient had no sexual experience.

The most common presenting symptom was urethral discharge with dysuria (68%) [Table 2]. Nearly 27% had only dysuria as the presenting complaint. The patients with discharge also had dysuria and burning micturition. Almost 15% had urethral discharge with coexisting genital ulcer disease (GUD). On examination of the genitalia, 68% had discharge per urethra (spontaneously presenting or with milking). Nearly 20% of patients had inguinal lymphadenopathy.

Almost 15% of the study population had coexisting genital ulcer. Five of these cases had VDRL positivity. Clinical diagnosis of ulcer disease was made. Eight cases were diagnosed as herpes genitalis. In three cases, clinical diagnosis of primary syphilis was made. In the remaining four cases, differential diagnosis of chancroid and syphilis was made.

Investigational reports

Gram’s staining of the smear showed Gram-negative diplococci in 40% of the patients. Nearly 33% were positive for culture for *N. gonorrhoea*. The results of PCR analysis are shown in Table 3. Both urine and urethral swabs were analyzed. *M. genitalium* was not detected from any specimen. *N. gonorrhoeae* was the most isolated organism. Urine and swabs showed similar results. In one case, urethral swab was positive for *C. trachomatis* but urine of the patient had negative result.

Table 2: Presenting symptoms

Presenting complaint	Number of patients
UD + dysuria	58
Dysuria	27
UD + dysuria + GUD	10
Dysuria + GUD	5

UD=Urethral discharge; GUD=Genital ulcer disease

Table 3: Polymerase chain reaction results of etiologic agents

Organism isolated	Number of patients
PCR <i>N. gonorrhoeae</i>	44
PCR <i>C. trachomatis</i>	13
PCR <i>M. genitalium</i>	0

PCR=Polymerase chain reaction; *N. gonorrhoeae*=*Neisseria gonorrhoeae*; *C. trachomatis*=*Chlamydia trachomatis*; *M. genitalium*=*Mycoplasma genitalium*

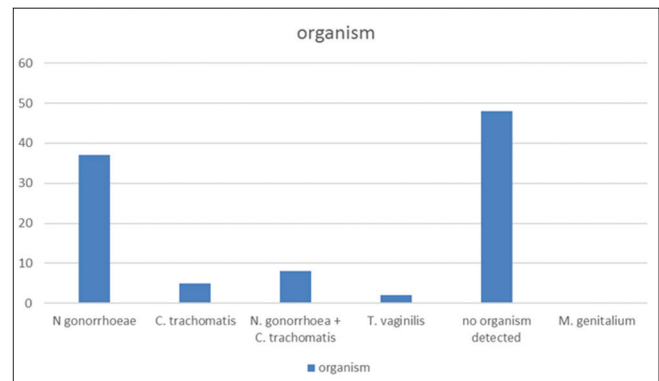
LED test showed color changes suggestive of positive results in 43 urine samples. Seventeen samples showed traces. Forty were negative. LED test which indicates the presence of PMNLs in the urine is a simple and inexpensive test.

N. gonorrhoeae was taken positive if detected by Gram’s stain, culture, or PCR (urine or swab). If any one of these was positive, the result was taken as positive. *C. trachomatis* and *M. genitalium* were tested by PCR. *T. vaginalis* was taken positive if found on wet mount or culture in the Inpouch TV. HIV infection was present in 10% of the study population. Etiological diagnosis among the study population is shown in Graph 1.

DISCUSSION

Urethritis is an important STD and forms a major chunk of the STD clinic attendees. Previously, urethral symptoms were predominantly discharge per urethra and frequency of micturition. *N. gonorrhoeae* was the only organism identified as the causative organism. Today, several organisms have been identified in the causation of urethritis including *Chlamydia trachomatis*, *Ureaplasma urealyticum*, *M. genitalium*, *T. vaginalis*, yeasts, herpes simplex virus, adenovirus, and *Hemophilus* species.^[1] Furthermore, the presentations and symptoms are changing. With the advent of HIV and AIDS, the atypical presentations of STDs are also observed. Mixed infection with two or more agents and multiple STDs is on the rise.

A study was conducted by Janier et al.^[2] to correlate the clinical presentation (urethral discharge or not), urethral swab, and first catch urine with the microorganisms found in the urethra. All their patients were screened for *C. trachomatis*, *N. gonorrhoeae*, *T. vaginalis*, *U. urealyticum*, *M. genitalium*, *Mycoplasma Hominis*, and *Candida albicans*. *C. trachomatis* was isolated in 13% of the



Graph 1: Etiologic agents isolated

patients. *M. genitalium* was detected in 17% of the patients. They concluded with the suggestion that a specific and sensitive search for *C. trachomatis* should be done in every patient with urethral symptoms, whether or not classic symptoms of urethritis are present.

In our study, 100 patients were recruited who had complaints suggestive of urethritis. The patients included in the study were aged between 16 and 50 years. The maximum number of patients was in the age group of 21–25 years. A study conducted by Alary *et al.*^[3] found the mean age of men with gonococcal or chlamydial infection to be 30.7 years. In the present study, the mean age of men presenting with urethritis was 33 years.

In the same study, among men with urethral discharge or dysuria, the most prevalent organism associated was *N. gonorrhoeae*^[3] which is comparable to our study; the most isolated organism was *N. gonorrhoeae* (37% alone and 8% co-infection with *C. trachomatis*).

Yet another study concluded *M. genitalium* as a common infection associated with symptomatic urethritis with a high prevalence of infected sexual partners, supporting its role as a sexually transmitted infection.^[4] Coexistence of multiple infections such as gonococcal urethritis, *C. trachomatis*, and *M. genitalium* necessitates syndromic management.^[5] The need for *T. vaginalis* treatment to be added to the syndromic management of urethritis was stressed.^[6]

In a study by Bhavsar^[7] on 113 cases of genital ulcerative disease and urethral discharge syndrome, the highest incidence of STDs was found in the age group of 20–40 years. The maximum number of cases was educated up to primary level. The maximum number of male STD cases was laborers (31.86%) and drivers (29.21%). About 34 (38.20%) cases had a history of exposure to female sex workers.

In our study, 55% of these patients had visited commercial sex workers at some point in their lifetime. About 84 patients (84%) had two or more sexual partners. Nearly 48% of the study patients were migrated, be it for work or study or other reasons. Almost 30% were unskilled laborers' group. In our study which recruited patients with symptoms of urethritis, it was found that 15% had coexisting GUD, whereas in another study, it was found to be as high as 53%.^[5]

In a study by Bhavsar, Patel, and Marfatia,^[7] out of 17 cases of UDS, purulent discharge suggestive of gonorrhoea was seen in 14 (82.34%) cases and all were validated by Gram-stain for gonococci.^[7] Mucoid discharge suggestive of nongonococcal urethritis was seen in three cases (17.64%), one case was found to be smear positive for gonococcus, and in the remaining two cases, laboratory confirmation was negative.

In the present study, all 45 cases with *N. gonorrhoeae* infection were associated with urethral discharge and dysuria. The same conclusion was drawn by Janier *et al.*^[2] Of the 13 cases positive for *C. trachomatis*, three cases had only dysuria. Two cases of *T. vaginalis* infection had urethral discharge [Table 4].

Jensen *et al.*^[8] compared the urethral swab and first catch urine for the diagnosis of *M. genitalium* and *C. trachomatis*. *M. genitalium* was positive in 6.8% of samples and *C. trachomatis* was detected in 13.3% of the patients. Their study showed that urine was better diagnostic specimen than urethral swab for the detection of *M. genitalium* and *C. trachomatis*. In our study, no one was positive for *M. genitalium* and 13% were positive for *C. trachomatis* (PCR technique). There was no significant difference between urine and swab specimens in our result. One urine sample remained negative for *C. trachomatis* while the corresponding swab was positive. In addition, one urine sample for *N. gonorrhoeae* remained negative while the corresponding urethral swab was positive. Since *M. genitalium* was not detected in any of the samples, it is proposed to be less prevalent in this part of the world. It is not as prevalent as in the Western countries.

In the present study, both culture and PCR for *N. gonorrhoeae* were positive in 32 (71%) cases. Only PCR was positive but culture negative for *N. gonorrhoeae* in 12 cases (26.6%). In one case, culture was positive but PCR remained negative.

Table 4: Comparison of various presenting complaints of urethritis in different studies

Presenting complaint	Janier <i>et al.</i> ^[2]	Present study
Discharge present	56%	68%
Discharge absent	44%	32%
Dysuria alone	16%	27%
Several symptoms (urethral itching, burning micturition, frequency, dysuria)	35%	-
Associated GUD	*	15%

*GUD was excluded from the study. GUD=Genital ulcer disease

These results show PCR to be a superior diagnostic tool. These results are comparatively similar to a study by Alary *et al.*,^[3] where of the 52 positive results, 14 were positive by both culture and PCR. About 35 samples were negative by culture but positive by PCR. [Table 5]

In the present study, 40 Gram-stained smears were positive for intracellular Gram-negative diplococci. This shows that Gram-stain still has importance and can be used to diagnose *N. gonorrhoeae* without much cost.

A comparison of different etiological agents causing urethritis detected in two other studies with our study is shown in Table 6. Janier *et al.* found *M. genitalium* as the most common etiological agent whereas Alary *et al.*, found *N. gonorrhoeae* as the most common etiological agent, which is similar to our study.

Both ulcerative and nonulcerative STDs are co-factors for the transmission of HIV. The emergence of HIV infection has increased the importance of measures aimed at the control of STDs.^[9] Improved case detection and management of patients presenting with STDs has shown to reduce the transmission of HIV. Trichomoniasis was associated with an increased risk of HIV transmission.^[10] The urethral inflammation and discharge help the transmission of HIV virus and thus increases the chance of HIV infection. Urethritis, of any etiology, increases the chances of acquiring HIV infection by the way of inflammatory cells, which phagocytose the virus and take them to systemic circulation. In addition, the breach in the mucosa of urethra facilitates easy entry

of the virus into the body. In our study, 10% of the cases tested HIV positive. However, window period may be a concern.

CONCLUSION

Urethral discharge with dysuria is still the most common symptom or presenting complaint in men with urethritis, as compared to Western countries where dysuria only, without frank discharge, is occurring more frequently. The rate of *N. gonorrhoeae* infection is still high in our setup, whereas *N. gonorrhoeae* infection rate has declined in Western countries. *C. trachomatis* is the second most common organism isolated. *T. vaginalis* was isolated in two patients. Hence, we have kept Trichomonas as a possible etiology of urethritis in our setup, not at all looked for as of now, and treat accordingly when suspected. PCR is a superior diagnostic tool compared to culture for *N. gonorrhoeae*. Nonspecific urethritis, where no organism is isolated, forms quite a part of the urethritis cases. HIV infection was present in 10% of the population studied. Educating the public, particularly the young, about safe sex and condom usage, needs to be greatly stressed upon. In addition, further studies are required to look for HSV in urethritis cases, which was not done in our study.

Acknowledgment

This study was supported by the Indo-Canadian HIV AIDS Project. We thank the support by the Department of Dermatology and Department of Microbiology, St. Johns Medical College, Bengaluru, Karnataka, India.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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Table 5: Comparison of culture and polymerase chain reaction-positive results for *Neisseria gonorrhoeae*

<i>N. gonorrhoeae</i>	Alary <i>et al.</i> ^[3]	Present study
Culture positive, PCR positive (%)	26.9	71
PCR positive, culture negative (%)	67	26.6

PCR=Polymerase chain reaction; *N. gonorrhoeae*=*Neisseria gonorrhoeae*

Table 6: Comparison of etiologic agents isolated in different studies

Organism detected	Janier <i>et al.</i> ^[2]	Alary <i>et al.</i> ^[3]	Present study
<i>N. gonorrhoeae</i> only (%)	10	39	37
<i>C. trachomatis</i> only (%)	12	7.6	5
<i>N. gonorrhoeae</i> + <i>C. trachomatis</i> (%)	1	5.8	8
<i>M. genitalium</i> (%)	17	Not done	0
<i>T. vaginalis</i> (%)	1	0	2
No organisms isolated (%)	35	-	48

N. gonorrhoeae=*Neisseria gonorrhoeae*; *C. trachomatis*=*Chlamydia trachomatis*; *M. genitalium*=*Mycoplasma genitalium*; *T. vaginalis*=*Trichomonas vaginalis*

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