

# Clinical characteristics of herpes simplex virus (HSV) urethritis, compared with chlamydial urethritis among men

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## Introduction:

Non Gonococcal Urethritis (NGU) in men, is a common sexually transmitted infection (STI), caused by *Chlamydia trachomatis* (20-50%), and *Mycoplasma genitalium* (up to 10-25%). *Trichomonas vaginalis*, adenovirus and Herpes simplex virus (HSV) account for less than 10%<sup>1,2</sup>.

## Aim of study:

To determine the clinical characteristics seen in men with HSV urethritis, to compare them, with those seen in men with chlamydia urethritis, and to determine if any key differences existed, that could guide testing for HSV in men presenting with NGU.

## Methods:

We compared clinical and laboratory data, from men with PCR confirmed HSV urethritis with that of men, with chlamydia urethritis.

### HSV Cases:

•All cases of male HSV PCR positive urethritis diagnosed at MSHC between January 2000 and September 2015, (n=80), that were identified at the laboratory VIDRL, and had a clinical diagnosis of NGU on their record.

### Chlamydia cases:

•Equal numbers of men, (n=80), diagnosed with chlamydia urethritis leading up to September 30th 2015.

All men had presented with symptoms suggestive of urethritis, (urethral discharge, discomfort and / or dysuria) and had a diagnosis of NGU entered on their record.

### Investigations for urethral pathogens:

•Urethral swab, where clinically indicated, for gram stain and *Neisseria gonorrhoea* culture (modified Thayer Martin medium).

•First passed urine (FPU) for *Chlamydia trachomatis* by strand displacement amplification (Probe Tec-ETCT amplified DNA assay; Becton, Dickinson) and *Mycoplasma Genitalium*3.

•FPU or urethral swab where clinically indicated for HSV by PCR targeting the glycoprotein gene using conventional PCR and a real-time version of this and / or Adenovirus by PCR targeting the hexon gene using conventional PCR and real-time PCR modified by Allard et al.

Differences between men with HSV and chlamydia urethritis were tested using the chi-square test or the Wilcoxon-Mann-Whitney test for categorical and continuous variables respectively.

## Results:

During the study period, 514 men were tested for urethral HSV and 80 men had PCR confirmed HSV urethritis. Of the 80 HSV cases, 55 (68% CI: 58-78) were caused by HSV-1 and 25 (32% CI: 22-44) by HSV-2, ( $p_{diff} < 0.01$ ). The majority of men (86%) had HSV diagnosed by urethral swab, and the remainder were by first passed urine. During the same period, there were 1,519 men diagnosed with chlamydia confirmed NGU; the last 80 were selected into the study.

The median age of men was similar in both groups, being 29 (IQR 24-38) for men with HSV urethritis, and 26 (IQR 23-31) for men with chlamydia urethritis ( $p_{diff} = 0.64$ ). Key differences in presenting symptoms and signs are compared in Table 1.

## Contact for more information

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Table 1: Frequency of clinical features and laboratory findings among men with HSV urethritis

	HSV urethritis (n=80)	Chlamydial urethritis (n=80)	p value
	No. (%; 95%CI)	No. (%; 95% CI)	
<b>Symptoms</b>			
Urethral discharge	14 (19, 11-27)	43 (54, 43-64)	<0.01
Urethral discomfort	37 (46, 36-57)	30 (38, 28-49)	0.26
Dysuria	60 (74, 64-83)	54 (67, 57-77)	0.30
Severe Dysuria	15 (20, 12-29)	0 (0, 0-5)	<0.01
Constitutional symptoms	11 (15, 8-23)	0 (0, 0-5)	<0.01
<b>Examination findings</b>			
Urethral discharge	25 (32, 22-42)	56 (69, 59-79)	<0.01
Meatitis	50 (62, 52-72)	17 (23, 14-32)	<0.01
Genital ulcer	29 (37, 27-47)	0 (0, 0-5)	<0.01
Inguinal lymphadenopathy	23 (30, 20-40)	0 (0, 0-5)	<0.01
<b>Laboratory findings</b>			
<i>Urethral microscopy</i>			
Performed	48	65	
0 PMNL/HPF	9 (19, 10-32)	7 (11, 5-21)	
1-4 PMNL/HPF	14 (29, 18-43)	19 (29, 20-41)	
≥5 PMNL/HPF	25 (52, 38-66)	39 (60, 48-71)	0.46
<i>Urethral gonorrhoea (culture)</i>			
Performed	53	61	
Positive	0 (0, 0-7)	0 (0, 0-6)	
<i>Urethral chlamydia</i>			
Performed	72	80	
Positive	4 (6, 2-13)	80 (100, 95-100)	
<i>Urethral Mycoplasma genitalium</i>			
Performed	55	78	
Positive	1 (2, 0-10)	0 (0, 0-5)	
<i>Adenovirus</i>			
Performed	44	0	
Positive	0 (0, 0-8)	0	

CI = Confidence interval, PMNL/HPF = polymorphonuclear leukocytes per high powered field

## Discussion:

Men with HSV urethritis, presented with distinctive clinical features, that were different from those found in men presenting with chlamydia urethritis. Men with HSV urethritis were significantly more likely to present with severe dysuria, constitutional symptoms, meatitis, lymphadenopathy and genital ulceration. And were significantly less likely to present with urethral discharge. A strength of this study, was that PCR was used throughout the testing period for HSV detection, providing for highly sensitive detection. Limitations included a possible bias towards certain clinical conditions as HSV testing was performed on clinical indications, however, the differences in clinical presentation were so marked that they are unlikely to be the results of selection bias alone.

## Conclusion:

HSV urethritis in men, was associated with distinctive clinical features, which are not usually associated with chlamydia urethritis. These include; severe dysuria, constitutional symptoms, meatitis, genital ulceration and lymphadenopathy. The presence of these symptoms and signs should alert clinicians to consider HSV testing.

## References:

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