



Kirti Nirmal<sup>1</sup>, Rumpa Saha<sup>2</sup>,  
Vishnampettai G Ramachandran<sup>3</sup>,  
Shukla Das<sup>4</sup>, Sambit Nath Bhattacharya<sup>5</sup>,  
Narendra Singh Mogha<sup>6</sup>, Iqbal Rajinder Kaur<sup>7</sup>

<sup>1</sup>Postgraduate Student, <sup>2,3</sup>Professor, <sup>4</sup>Dir. Professor, <sup>6</sup>Sr. Technical Assistant, <sup>7</sup>Dir. Professor & Head, Department of Microbiology, <sup>5</sup>Dir. Professor & Head, Department of Dermatology Venereology and Leprology, University College of Medical Sciences and GTB Hospital (Delhi University), Delhi, India.

**Correspondence to:**

Dr. Rumpa Saha, Professor, Department of Microbiology, University College of Medical Sciences and GTB Hospital (Delhi University), Delhi, India.

**E-mail Id:**

rumpachatterjee@yahoo.co.in

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## Co-Infection of HSV in Gonococcal Urethritis Patients

### Abstract

Co-infection with two different pathogens may alter the classical clinical course that manifests infection as single pathogen. In STIs, such co-infection may trigger the reactivation of a latent infection, and syndromic approach may not be insufficient to free the host of the entire gamut of infectivity agents. Present study analyzed appropriate samples for *Neisseria gonorrhoeae* and HSV from 200 patients presented to STI clinic. Gonorrhoea was detected in 4% and HSV in 5% of patients. 25% of gonorrhoea patients had HSV-2 co-infection with an overall 4.5% yield of subclinical HSV cases which would have been missed leading to inappropriate treatment, risk of recurrence and transmission to contacts. Awareness regarding encounter with multiple infections is necessary for effective management.

**Keywords:** STIs, Neisseria Gonorrhoeae (GC), Herpes Simplex Virus (HSV).

### Introduction

The emerging pandemic of AIDS has focused on STI control as one of the important strategies to curb HIV transmission in community. Co-existence of one STI with viral or bacterial agent may change the classical behavior of the genital infection and may provide the stimulus for reactivation of a latent pathogen.<sup>1</sup> Epidemiologic and laboratory research demonstrate that ulcerative STIs facilitate HIV transmission.<sup>2</sup> Syndromic approach, especially in cases of co-infection, may not be sufficient to eliminate with certainty STI-causing organisms from the host.<sup>3</sup> Among the STIs, *Neisseria gonorrhoeae* (GC) is a significant public health problem with about 106 million annual cases occurring worldwide. It is a successful pathogen with a remarkable journey over the years.<sup>4</sup> Empirical observation on dual infection with *N. gonorrhoeae* and HSV at our center stimulated a literature search and paucity of reports on co-infection with these agents led us to determine co-infection with HSV and *N. gonorrhoeae* in patients attending STI clinic of our tertiary hospital in north India.

### Materials and Methods

Two hundred consecutive patients attending our STI clinic between Nov 2013 and April 2015 with complaints of genital ulcer or discharge were investigated by Gram stain and/or Giemsa stain (impression Tzanck smear) for intracellular Gram-negative diplococci (ICDC) suggestive of GC and multinucleated giant cell (MNGC) suggestive of HSV. GCs were isolated on chocolate agar (CA) base with hemoglobin and vancomycin, colistin, nystatin and trimethoprim (VCNT) supplements (HI-media, India) followed by their antimicrobial susceptibility testing with penicillin (0.5 IU), tetracycline (10 µg), ceftriaxone (0.5 µg), spectinomycin (100 µg), ciprofloxacin (1 µg), naladixic acid (30 µg), azithromycin (15 µg), and cefpodoxime (10 µg) (Oxoid, U.K). Penicillinase producing *N. gonorrhoea* (PPNG) was detected by chromogenic cephalosporin method. MIC of ceftriaxone was estimated by E-strips containing 0.002–32 µg/mL (Hi-Media, India). HSV-1 IgM (Maddens Diagnostics HSV-1 Netherlands) and HSV-2 IgM (Ridascreen HSV-2 IgM Germany) as well as HIV antibodies as per NACO guidelines were detected with three different rapid test kits employing different strategies for detection of the analyte.

## Results

Although total females outnumbered their counterparts (M:F = 1:7.4) in the present study, a prevalence of 4% gonorrhoea (8 cases) was detected more in males. AST of *N. gonorrhoeae* isolates showed 5 isolates were resistant to penicillin, one of which was penicillinase producing *N. gonorrhoeae* (PPNG). The PPNG isolate was also resistant to naladixic acid and ciprofloxacin. Two isolates were tetracycline-resistant *N. gonorrhoeae* (TRNG) but were

sensitive to other antibiotics. None had elevated MIC to ceftriaxone. In the present study, the overall prevalence of genital herpes was 5% (10 cases with a male: female ratio of 1:4). HSV-1 was detected in 1.5% and HSV-2 in 3.5% and simultaneously presence of both HSV1 and 2 was detected in 2.5% cases. Twenty-five percent of gonorrhoea patients had HSV-2 co-infection and a statistically significant association (Fischer exact test,  $P=0.039$ ,  $df=1$ ) was noted between the two.

Table 1. Results

|       |       | <i>N.gonorrhoea</i> |     | Total | Test, df, P value                         |
|-------|-------|---------------------|-----|-------|---|
|       |       | (-)                 | (+) |       |   |
| HSV-2 | (-)   | 187                 | 6   | 193   | Fischer exact test<br>$P=0.039$<br>$df=1$ |
|       | (+)   | 5                   | 2   | 7     |   |
|       | Total | 192                 | 8   | 200   |   |

## Discussion

Prevalence of gonorrhoea in different regions of India varies from 3 to 19%.<sup>5</sup> However, there has been a decline of this STI over the past decade as is evident in the present study (4%) and reports from Chandigarh<sup>6</sup> and Patiala,<sup>7</sup> probably due to the availability of medical facilities including syndromic management of STIs in peripheral health care level and private health setups. The overall prevalence of HSV-2 in our study was very low (5%) as compared to higher prevalence of 28.7% and 32.7% in two previous studies from the same institutions eight and six years ago respectively.<sup>8,9</sup> A high prevalence of genital herpes has also been reported from Kerala.<sup>10</sup>

Twenty-five percent of our gonorrhoea patients had co-infection with HSV-2 which is much higher compared to an earlier study (0.3%).<sup>11</sup> However, the typical ulcerative presentation of genital herpes was not seen in these co-infections. HSV-2 infection was detected serologically enlightening a subclinical HSV co-infection rate of 25%. The overall subclinical HSV infection was 4.5%. WHO treatment regimen currently in use would have missed 9 cases of primary genital HSV infection leading to inappropriate treatment. Such a delay in diagnosis can nevertheless lead to grievous consequences, especially in the immunosuppressed or in cases of vertical transmission. In the present study, 70% of HSV-positive subjects were females in the reproductive age group and can act as potential transmitters to their off-springs. Moreover, transmission of infection to their sexual partners may further aggravate the situation. Thus detection of subclinical HSV co-infection by serology not only facilitates initiation of appropriate treatment but also reduces the risk of recurrence and HSV

transmission to contacts. A study from Saudi Arabia, where primary HSV infection co-existed with *N. gonorrhoeae*, only 4.7% cases had typical ulcerative lesion of genital herpes.<sup>4</sup> It is interesting to note that in our patients with GC and HSV co-infection, 12.5% of them had HIV sero-positivity also.

Thus, clinicians are encouraged to be aware of co-infections with two or more STI pathogens, where one of them may be latent and awaiting a trigger for reactivation, thereby alternating the robustness of this infection efficiency by syndromic approach to STI co-infections (single/ multiple). Necessary modification may be adapted as per the epidemiological pattern of STIs in a given setting. A comprehensive knowledge of the various epidemiological factors including appropriate screening measures is essential to design proper preventive and control strategies to curb STIs.

**Conflict of Interest:** None

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