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Etiological profile of genital ulcer disease in patients attending a regional center for sexually transmitted infections in central India: A 5 years analysis (2017-2021)

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Abstract

Background: Sexually transmitted infections (STIs) are becoming a major public health problem in developing countries worldwide. Proper history and perfect laboratory diagnosis is important for complete cure of patients.

AIM: Aim of the presenting study is to determine the etiological profile of genital ulcers in patients attending with Genital Ulcer Disease (GUD) in a regional STI clinic at tertiary care hospital in central India.

Material and Methods: Swabs & serum were collected at Regional STI center, Govt. Medical College & Hospital, Nagpur, from 780 patients of GUD between April 2017 to March 2021, for determining the etiology. Staining techniques used were Gram, Giemsa and Dark Ground Illumination (DGI). Serum IgG and IgM against *Herpes simplex virus- type 2* (HSV-2) were determined by ELISA and specific anti treponemal antibodies of *Treponema pallidum* were determined by hemagglutination (TPHA) test.

Results and Discussion: Out of 780 patients, 621 were male and 159 were female. Etiology could be determined in 333(42.69%) patients. HSV-2 infection accounted for 231 (26.61%) cases, 58 (7.4%) by staining, 127 (16.2%) being IgG positive and 79 (10.1%) being IgM positive. *T. pallidum* was responsible for 42 (5.38%) cases by TPHA including 3 (0.3%) cases by DGI. *Haemophilus ducreyi* was identified in 40 (5.12%) and *Calymmatobacterium granulomatis* in 20 (2.56%) cases both by staining. Lymphogranuloma venereum (LGV) infection did not present as ulcer but as bubo in 4 (0.51%) patients.

Conclusion: In our region herpes due to HSV-2 was the commonest GUD followed by syphilis, chancroid and donovanosis in that order.

Keywords: Chancroid, donovanosis, genital ulcer disease, herpes, syphilis

Introduction

Genital Ulcer Disease (GUD) represents a diagnostic dilemma especially in India. Access to reliable laboratory facilities is restricted in India. An accurate diagnosis is needed for appropriate treatment and formulation of control policies. Sexually transmitted infections (STIs) are becoming a major public health problem in developing countries worldwide [1]. Near about 187 million people in world had at least one episode of HSV related GUD in their lifetime [2].

Genital ulcer disease is clinically classified as herpetic and non-herpetic. Non-herpetic group include syphilis, chancroid and donovanosis while herpetic group include herpes simplex virus. Herpes simplex virus can cause painful and recurrent genital ulcers. For GUD detailed medical history, physical examination and correct laboratory diagnosis is essential for management of patient [3].

According to World Health Organization (WHO), every year nearly 10-12 million new infections of syphilis occur. There are four stages of syphilis i.e., early or primary, secondary, latent and tertiary stage. It increases from painless ulcers to gummas with involvement of lymph nodes. Chancroid is also one of the common genital ulcer diseases in sexually transmitted infections and it is caused by *Haemophilus ducreyi*.

Prevalence of chancroid is nearly 9.9%-34.7% in India. Chancroid is most prevalent in developing countries of Asia, Africa and latent America among the people of low socioeconomic status.

The incidence of Donovanosis varies from 0.3% to 23.6% across India [4]. Donovanosis characterized by granulomatous ulcers of genitalia caused by *Calymmatobacterium granulomatis*, a Gram-negative pleomorphic bacterium.

The present study was undertaken to determine the etiology of genital ulcer disease in patients attending the regional STI center in central India.

Material and Methods

The study was conducted in the Regional STI Training, Research and Referral Laboratory (RSTRRL) located in the Department of Microbiology, GMC Nagpur.

The patients attending the STI clinics in the affiliated clinical department of Skin and VD and Obstetrics and Gynaecology were included in the study during the period of April 2017-2021. A total of 780 non-replicated patients presented with GUD were included in the study.

1) Sample collection

Swabs were collected from genital ulcers after cleaning with sterile normal saline. The lesion was rubbed with sterile gauze piece till it bled. The serous fluid which oozed was taken on the slide or on a thin sterile capillary tube.⁵

2) Microscope

Gram stain

- Gram staining identified *Haemophilus ducreyi* as a gram-negative coccobacillus seen either as school of fish or rail road track or fingerprints with plenty of segmented neutrophils.

Giemsa stain

- Giemsa staining identified Donovan bodies seen as large mononuclear cells of size 0.5-0.7 by 1-1.5µm full of short, stout, capsulated coccobacilli pushing the nucleus to periphery in a case of Donovanosis.

- Large multinucleated Giant cells with faceted nuclei were diagnosis of herpes simplex infection.

Dark field microscopy (DFM)

- Dark field microscopy identified *Treponema pallidum* as a motile, silvery, white, thin, spiral organism of size 6-14 µm long.

3) Serology

Syphilis serology test was done by Venereal Disease Research Laboratory (VDRL) slide flocculation test. The antigen was procured from The Institute of Serology, Calcutta. Samples with VDRL titer >1:8 were confirmed by *Treponema pallidum* Haem Agglutination (TPHA) test using PLASMATEC kit which was procured from L21 Healthcare limited Dorset, DT6 5BU United Kingdom. Both tests were performed as per manufacturer's instructions.

IgM and IgG antibodies to HSV-2 were determined by Enzyme Linked Immunosorbent Assay (ELISA) method using NOVATECH Immundiagnostica GmbH kit, WaldstraBe 23 A6, 63128 Dietzenbach, Germany.

Results

Out of 780 patients of GUD, 206 patients presented with non-herpetic GUD while 574 presented with herpetic GUD (Table). Etiology could be determined in 333(42.69%) patients. Syphilis was diagnosed in 42 (5.38%) patients that were serologically positive both by VDRL and TPHA. This included 3 patients that were positive by DFM. Chancroid was diagnosed in 40 (5.1%) patients and Donovanosis in 20 (2.6%) patients both by microscopy alone.

Among the 574 clinically diagnosed herpetic patients, microscopy alone was positive in 25 patients while microscopy and serology was positive in 33 patients (21 were HSV-2 + IgG positive, and 12 were HSV-2 + IgM positive). 4 out of 58 microscopy positives were positive for both HSV-2 IgG and HSV-2 IgM.

Lymphogranuloma venereum (LGV) infection was not encountered as ulcer but presented as bubo in 4 (0.51%) patients.

Table 1: Etiology of Genital Ulcer Disease (2017-2021)

S. N.	Clinical Gud	No. Of Samples*	Microscopy** (%)	Serology (%)				Positive Patients
				VDRL	TPHA	IgG	IgM	
Non-herpetic								102
1.	Syphilis		3(0.3)	42(5.38)	42(5.38)	-	-	
	Chancroid	206	40(5.12)	-	-	-	-	
	Donovanosis		20(2.56)	-	-	-	-	
Herpetic								231
2.	HSV-2	574	58(7.43)	-	-	127(16.2)	79(10.1)	
	Total	780	121(15.5)	42(5.38)	42(5.38)	127(16.2)	79(10.1)	
Total Positive Gud Patients								333 (42.69)

*Male- 621, Female- 159.

**Microscopy- Syphilis identified by DFM, Chancroid identified by Gram stain, Donovanosis and HSV-2 identified by Giemsa stain.

Discussion

A total of 780 patients were included in the study. The prevalence of genital ulcer diseases world over has ranged from 5.0%-65.2% [6, 7, 8] whereas in India the reported range is 7.45%-62% [3, 9, 10, 11]. In the present study, the prevalence for Genital Ulcer Disease was 42.69% (Table). Predominance of males in GUD has been reported, most of

the patients belonging to age group of 20-30 years [1, 9, 12]. In present study also male predominance was observed, male to female ratio was 4:1. Most of the patients belonged to low socio-economic class.

A marked increase in viral STIs as compared to bacterial STIs has been reported in various regions of India. This may be due to increasing use of broad-spectrum antimicrobials

purchased over the counter and self-medication without reporting to medical facilities for proper diagnosis and treatment as STIs are associated with social stigma¹. We found Herpes Simplex Virus-2 to be the commonest infection among Genital Ulcer infections (26.61%). Similar finding has been reported by Choudhry S *et al.*^[9], Kumar *et al.*^[12] from India and Naveca F G *et al.*^[6] from Brazil. The increasing prevalence of genital herpes infection varies worldwide. HSV-2 seroprevalence in the USA has increased by 30% since 1970s, with the result that in recent years the infection is seen in one out of five adults.

We found syphilis to be the second commonest cause of ulcerative STIs. In screening for early syphilis, VDRL test is important. The test should be repeated over a period of at least 3 months^[13]. In the present study, confirmatory TPHA reactivity was seen in 5.38% of total ulcerative STI patients. TPHA reactivity of 9.41% has been documented by Vora R *et al.*^[14] and 11.2% by Choudhry S *et al.*^[9]. We found a positivity of 5.38% by both VDRL and TPHA tests. False positivity in VDRL was rare in our patients may be due to correct patient selection. However, Robertson *et al.*^[13] reported 6 cases of syphilis by TPHA test that would not have been detected by VDRL test. Prevalence of syphilis in India varies from 5% to 6%^[10, 15, 16] while worldwide it varies from 4% to 7.5%^[17, 18, 19].

Chancroid is encountered very rarely in most developed and much developing countries now¹⁶. This is because in the last three decades there was an extensive use of syndromic approaches for the management of STIs caused by bacterial pathogens, which resulted in rapid decline of chancroid. In India patients of chancroid have shown a downhill pattern. In our study chancroid accounted for 40 (5.1%) out of 780 patients. Our findings are comparable to other studies that have reported 3.3% by Murlidhar *et al.*^[3], 3% by Rapp EH *et al.*^[20] and 1.05% by Bachaspatimayum R *et al.*^[11]. Worldwide prevalence of chancroid ranges from 3.3% to 15.2%^[7, 21, 22]. A study of GUDs in Zambia yielded 0% prevalence of *H. ducreyi*^[3] No case of *H. ducreyi* has been reported from Australia since 1998.

Donovanosis is a chronic cause of genital ulcers. It was first described in New Guinea, America^[6]. It is most well known in south-east India. In the present study 2.6% cases of donovanosis were confirmed by Giemsa staining. Almost similar results were found by Muller EE *et al.*^[8] (2.0%) and Kumar *et al.*^[12] (1.35%). Australian government publication data reported a declining pattern in cases of donovanosis with an initial data of 117 cases in 1994 to 12 cases in 2000 and now a complete eradication of Granuloma inguinale (GI)^[23]. In India, the states of Orissa, Andhra Pradesh and Tamil Nadu have recently reported 6 new cases of GI in immuno compromised patients^[23].

In our study we did not get any case of ulcer due to lymphogranuloma venereum (LGV) although 4 patients presented with bubo and the bubo aspirate was positive for chlamydia trachomatis by direct fluorescent antibody test. Ulcers are formed in untreated cases of bubo. This indicates that LGV infections cannot be ruled out as a cause of genital ulcers in our region.

Conclusion

In our region herpes due to HSV-2 was the commonest GUD followed by syphilis due to *T. pallidum*. Chancroid due to *H. ducreyi* was uncommon. Donovanosis due to

Klebsiella granulomatis was rare. Ulcer due to LGV though not encountered cannot be ruled out.

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Conflict of interest: None.

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