

Trends in genital ulcer disease: An observational study at a tertiary care teaching hospital

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Abstract

Introduction: Genital ulcer disease (GUD) often creates diagnostic difficulty in developing countries like India, with limited resources available in the health-care system. The changing etiology in GUDs over the years makes it imperative that a correct diagnosis is made to establish appropriate treatment and formulate awareness programs. **Aims:** This study was done to determine the recent trends in the demographic parameters, clinical presentations, etiology of GUDs, and their association with human immunodeficiency virus (HIV). **Materials and Methods:** An observational cross-sectional study was conducted from October 2021 to August 2022 at the Dermatology Outpatient Department in our hospital. All the patients who presented with GUDs were included after written informed consent. The diagnosis of GUD was confirmed by thorough clinical examination and appropriate laboratory test. Data were entered and analyzed using IBM SPSS software. **Results:** Out of 135 cases of GUDs, the majority were males (79%). The most common age group was 21–30 years, with a mean age of 35.23 ± 14.98 years. Most of the patients were heterosexual (90%). Multiple sexual partners were found in 40% of cases. Herpes genitalis was the most common GUD (59%), followed by syphilis (15%). HIV infection was found in 6.6% of cases. **Conclusion:** This study represents the increasing burden of viral GUDs compared to the last three decades. The ulcerative sexually transmitted infection facilitates the transmission of HIV. In this HIV era, there is a need for increased efforts toward acknowledgment, safe sexual practices, periodic screening, and sexual health awareness programs in the high-risk population.

Key words: Genital ulcer disease, herpes genitalis, heterosexual, human immunodeficiency virus, syphilis

Introduction

Any ulcerative condition of the genitals can be included under the term genital ulcer disease (GUD). A genital ulcer is defined as a breach in the continuity of epithelium in genital mucosa and skin.^[1] Genital ulcers may be caused by venereological and nonvenereological etiologies. Venereological causes include genital herpes, syphilis, chancroid, donovanosis (granuloma inguinale), and lymphogranuloma venereum (LGV). Nonvenereological causes include trauma, various drug reactions, Behcet's disease, and vesiculobullous disease. Data from multiple studies across the world exhibit that the annual global incidence of GUDs exceeds 20 million cases.^[2] The proportion of GUD is very high among sexually transmitted disease (STD) patients, with 50%–60% of patients having GUD.^[3,4] GUDs have a significant impact on morbidity and mortality in all STDs, partially because of their ability to enhance the rate of sexual transmission of human immunodeficiency virus (HIV).^[5,6] Very few studies have shown the regional burden of ulcerative STDs in recent years.

Aims and objectives

This study was done to determine the recent trends in the demographic parameters, clinical presentations, etiology of GUDs, and their association with human immunodeficiency virus (HIV).

Materials and Methods

Study design and ethical approval

An observational cross-sectional study was conducted from October 2021 to August 2022 at the outpatient department of a tertiary care hospital in Surendranagar, Gujarat. Ethical approval was obtained from the Institutional Ethics Committee of the C.U. Shah Medical College with reference no. IEC-HR, CUSMC/Im/39/2022, dated March 22, 2022.

Inclusion criteria

The patients clinically diagnosed as GUDs attending the Dermatology Outpatient Department were included after

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How to cite this article: Patel ZR, Makwana VS, Bhadja SG, Tundiya HJ, Vyas AP. Trends in genital ulcer disease: An observational study at a tertiary care teaching hospital. *Indian J Sex Transm Dis* 2023;44:121-7.

Submitted: 27-Dec-2022

Revised: 15-Feb-2023

Accepted: 14-Apr-2023

Published: 06-Dec-2023

Access this article online

Quick Response Code:



Website:

www.ijstd.org

DOI:

10.4103/ijstd.ijstd_125_22

written informed consent. In females, the ulcers over mons pubis, labia minora, labia majora, vaginal introitus, posterior commissure, and perianal area were included. In males, the ulcers over the glans penis, coronal sulcus, shaft of the penis, scrotum, perianal area, and urethral meatus were included.

Methodology

Each patient was subjected to a detailed history, including age, gender, marital status, education, socioeconomic status, and occupation. A thorough history of sexual exposure, sexual partners, and sexual orientation was noted. Chief complaints, duration, previous treatment history, and clinical diagnosis were recorded. We inspected ulcerative lesions for size, shape, number, color, symmetry, margin, floor, edges, and discharge and palpated to examine tenderness and induration. In all patients, systemic examination and lymph node palpation were done.

Diagnostic tests

HIV antibody testing by immunodot method was performed in every patient.

To diagnose syphilis, we performed rapid plasma reagin (RPR) test in all patients and treponema pallidum hemagglutination test whenever required. For detecting *Haemophilus ducreyi*, smears were taken with cotton swabs from beneath the undermined edge of ulcers, and Gram stain was performed. In Gram stain, the arrangement of pleomorphic Gram-negative coccobacilli in parallel chains of two's or four's "school of fish" appearance was considered diagnostic of chancroid.^[7]

The presence of LGV was confirmed by performing the Giemsa stain on the swab taken from the base of ulcer and bubo aspirates. Purple staining elementary bodies and blue staining reticulate bodies were taken as diagnostic.^[8]

In patients with herpes genitalis, Tzanck smear was prepared and the presence of multinucleated giant cells and acantholytic cells were taken as confirmatory for herpes genitalis.

Anti-herpes simplex virus (HSV)-1 and anti-HSV-2 immunoglobulin (Ig) M, and IgG antibody tests were done in these patients using captured enzyme-linked immunosorbent assay (ELISA) whenever required.

Potassium hydroxide (KOH) mount was done to detect *Candida* infection. On KOH preparation, the presence of budding cells and pseudohyphae was taken as diagnostic. Complete blood count, random blood sugar, and urine routine and microbiological examination were done as and when required].

Statistical analysis

Data were entered and analyzed using SPSS software (Version 26). SPSS Version 26 (IBM CROP. Released 2019. IBM SPSS Statistics for windows, Version 26.0. Armonk, NY: IBM Crop)

We applied the Chi-square test, Fisher's exact test, and Mann-Whitney *U*-test on variables to determine the association between variables and HIV status.

Results

During the study period of October 2021 to August 2022, 20,441 patients attended the Dermatology Outpatient Department at our tertiary care teaching hospital. Out of 20,441 patients, 135 patients were diagnosed with GUD. Therefore, the prevalence of GUD in our region is 0.66%.

The patients' ages ranged from 18 to 70 years, with the majority belonging to 21–30 years 32% ($n = 43$),

followed by 31–40 years 26% ($n = 29$). The mean age was 35.23 years \pm 14.92 [Table 1]. Male patients outnumbered female patients. Seventy-nine percent ($n = 107$) of patients were male, and 21% ($n = 28$) of patients were female, with a male-to-female ratio of 4:1 [Figure 1].

In our study, most of the patients were residing in rural areas, 61% ($n = 83$). Out of 83 patients living in rural areas, five patients showed HIV positivity, and out of 52 patients residing in the urban area, four patients showed HIV positivity. However, this finding was not statistically significant ($P > 0.05$). Fifty-eight percent ($n = 78$) of patients were educated up to the primary level, while 42% were educated up to secondary education. Most patients were manual workers, 58.51% ($n = 79$), followed by homemakers, office workers, students, business people, and shopkeepers. In the Modified Kuppuswamy Scale,^[9] most of our study participants belonged to the lower middle class, 44% ($n = 60$), followed by the upper lower, lower, upper middle, and upper classes. We did not find any statistically significant association between these demographic variables and HIV positivity ($P > 0.05$) [Table 1].

In most of the cases, 67% ($n = 90$) presented within 7 days of onset. The mean duration of GUD in our study group was 6.61 days [Table 2].

Most of them were heterosexual 90.3% ($n = 122$), followed by homosexual 5.2% ($n = 7$), bisexual 3.7% ($n = 5$), and sexually inactive 0.74% ($n = 1$). Out of nine HIV-positive patients, eight were heterosexual, and one was bisexual. This difference was not statistically significant ($P = 0.99$). A history of multiple sexual partners was found in 29% ($n = 40$) of patients. All HIV-positive patients had a history of multiple sexual partners. Fisher's exact test showed statistical significance between multiple sexual partners and HIV positivity among patients of GUDs ($P < 0.05$).

Furthermore, only 16% ($n = 21$) of patients used barrier contraceptives. Out of nine patients with HIV, six patients were not using any barrier contraception, but no significant association was found between contraception use and HIV positivity [Table 3].

Out of 135 patients of GUD, 22% ($n = 30$) had nonvenereological etiology, while 78% ($n = 105$) had venereal diseases [Figure 2]. The most common GUD was herpes genitalis, 59% ($n = 80$) among all GUDs and the venereological group. Other sexually transmitted

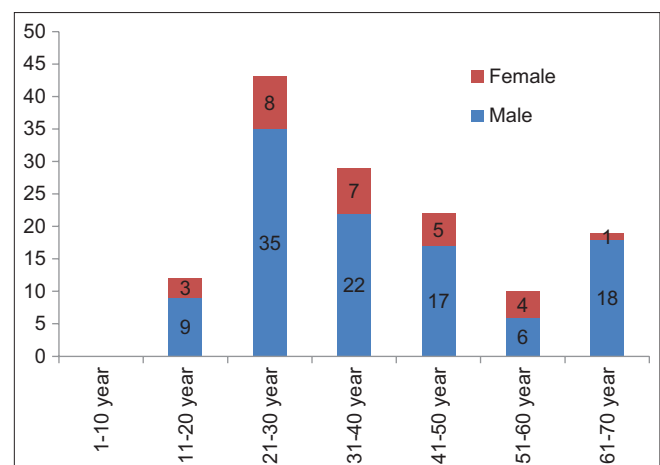
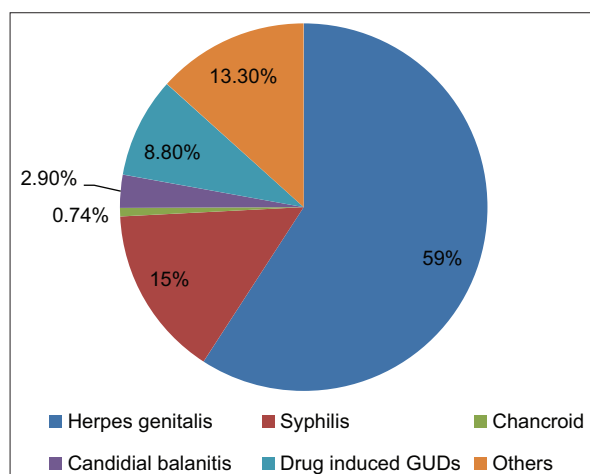


Figure 1: Age- and gender-wise distribution of study participants

Table 1: Sociodemographic profile of study participants

Variable	n (%)	HIV positive (n=9)	HIV negative (n=126)	HIV positive versus HIV negative (P)
Mean age (years)	35.23	-	-	
Residence				
Rural	83 (61)	5	78	0.97 (>0.05)
Urban	52 (39)	4	48	
Educational status				
Primary education	78 (58)	4	74	0.62 (>0.05)
Secondary education	57 (42)	5	52	
Occupation				
Manual worker	79 (58.57)	5	74	0.86 (>0.05)
Others	56 (41.48)	4	52	
Socioeconomical status (Modified Kuppuswamy Scale) ^[9]				
Upper class	2 (1.5)	-	2	0.83 (>0.05)
Upper middle class	8 (6)	1	7	
Lower middle class	60 (44)	3	57	
Upper lower class	50 (37)	3	47	
Lower class	15 (11)	2	13	

HIV=Human immunodeficiency virus

**Figure 2: Types of GUDs among the study participants. GUD = Genital ulcer disease****Figure 3: Syphilitic ulcer**

GUDs found were syphilis 15% ($n = 20$) [Figure 3], chancroid 0.74% ($n = 1$) [Figure 4], and *Candida* balanitis 2.96% ($n = 4$) in the present study [Table 3].

In nonvenereological GUDs, drug-induced GUD 8.8% ($n = 12$) [Figure 5] was the most common entity detected. Other causes of nonvenereological GUDs were traumatic 5.9% ($n = 8$), pemphigus vulgaris 4.4% ($n = 6$) [Figure 6], squamous cell carcinoma 1.5% ($n = 2$) [Figure 7], Behcet's disease 0.7% ($n = 1$), and Zoon's balanitis 0.7% ($n = 1$) [Figure 8].

In our study, we performed HIV testing, RPR testing, Tzanck smear/Giemsa stain, and Gram stain in all patients. Seven percent ($n = 9$) of patients and 15% ($n = 20$) of patients were found positive for HIV and RPR, respectively. Five patients with herpes genitalis and three patients with syphilis tested positive for HIV. The association between the type of GUD and HIV positivity was statistically significant ($P < 0.05$) [Table 3].

Out of 80 clinically suspected as herpes genitalis [Figure 9], 70% ($n = 56$) of patients showed multinucleated giant cells and acantholytic cells in the Tzanck smear/Giemsa stain [Figure 10]. KOH examination was performed in four patients of candidal balanitis,

in which two patients showed budding cells and pseudohyphae [Figure 11].

Discussion

Bacterial GUDs were the most common in the 1970s. However, by the 1980s, with the emergence of HIV infection, viral GUD became more common.^[10] Various studies revealed that viral GUDs had increased right now. Genital herpes is the most common cause of genital ulcers worldwide.^[11] Sexually transmitted genital ulcer constitutes a significant portion of overall GUDs and increases the burden of STDs. STDs cause substantial morbidity, mortality, and stigma. Hence, proper diagnosis is required to initiate the treatment and control the disease.

In our study, we had 135 patients with GUDs.

Most cases were male, 79% ($n = 107$), with a male-to-female ratio of 4:1. A similar result was also observed in Setia *et al.*,^[12] with males 87.35% and females 11.8%, and Muralidhar *et al.*,^[13] with males 66.7% and females 33.3%, but different results were found in Nyati *et al.*,^[14] males 38% and females 62% [Table 4]. Males outnumbered females in our study. Males more frequently leave their homes for job opportunities, which makes them more prone to exposure to multiple sexual

partners, including commercial sex workers. Females in our community hesitate to come forward for diagnosis due to social, cultural, and religious stigma and lack of knowledge.

Most cases of GUDs were between 21 and 30 years, 32% ($n = 43$) [Figure 1], which was nearly similar to Setia *et al.*,^[12] Muralidhar *et al.*,^[13] and Nyati *et al.*^[14] The mean age found in our study was 35.23 ± 14.98 years [Table 1]. The mean age was 34 years in a study done by Hope-Rapp *et al.*^[16] This age group is a sexually active age group. There has been a change in sexual practices in recent years because the initiation of sexual activities started earlier as compared to previous years in the young generation.

In our study, more than half of the patients reside in a rural area, 61% ($n = 83$), which contrasts with Nyati *et al.*,^[14] 36.2% ($n = 1756$). This difference in our study between rural and urban patients could be due to their lack of health education and awareness. Among the 135 patients, the majority were educated up to primary education, 58% ($n = 78$). Nyati *et al.*^[14] also showed that the majority of patients were below the secondary education, 54% ($n = 2615$). Regarding occupation, most patients, 58.57% ($n = 79$), were manual workers. This finding was similar to the study done by Bhavsar *et al.*^[17] Laborers and truck drivers were found to be a high-risk group for transmitting GUDs.

According to socioeconomic status (Modified Kuppuswamy Scale),^[9] majorities belonged to the lower middle class, 44% ($n = 60$), followed by upper-lower class,

37% ($n = 50$). Jayasree *et al.*^[18] mentioned in their study that the majority of patients were from the upper middle class, 59% ($n = 36$), followed by the lower middle class, 22% ($n = 36$), which differed from our study.

In our study, more than half of the patients, 67% ($n = 90$), had a disease duration of 1–7 days. The mean duration was 6.61 days. In contrast, a study done by Prabhakar *et al.*^[19] showed that 39.7% ($n = 77$) of cases had a duration of 30 days, and 23.2% ($n = 45$) had 1–7 days.

A total of 90% ($n = 122$) of patients had a heterosexual orientation, while 5% ($n = 7$) had a homosexual orientation, 4% ($n = 5$) of patients had a bisexual orientation and 1% ($n = 1$) of patients were sexually inactive. Muralidhar *et al.*^[13] reported that 98.2% ($n = 89$) of patients were heterosexual, 2% ($n = 1$) of patients were homosexual, and none were bisexual. Nyati *et al.*^[14] showed that 97.3% ($n = 4718$) of patients belonged to the heterosexual category, 1.6% ($n = 76$) of patients belonged to the

Table 2: Duration of genital ulcer diseases

Duration (days)	Number of patients, n (%)
1-7	90 (67)
8-14	22 (16)
15-30	17 (13)
>30	6 (4)
Mean duration	6.61



Figure 4: Chancroid ulcer

Table 3: Sexual behavior of study participants

Characteristics	n (%)	HIV positive (n=9)	HIV negative (n=126)	HIV positive versus HIV negative (P)
Sexual orientation (n=135)				
Heterosexual	122 (90.3)	8	114	0.99 (>0.05)
Homosexual	7 (5.2)	0	7	
Bisexual	5 (3.7)	1	4	
Sexually inactive	1 (0.74)	0	1	
Nature of sexual contact (n=134)				
Single partner	94 (70)	0	94	0.00001 (<0.05)
Multiple partners	40 (30)	9	31	
History of use of protection condoms (n=134)				
Unprotected	113 (84)	6	107	0.3 (>0.05)
Protected	21 (16)	3	18	
Type of GUDs				
Total number of GUDs	135 (100)			0.0325 (<0.05)
Venereological GUDs				
Herpes genitalis	80 (59)	5	75	
Syphilis	20 (15)	3	17	
Chancroid	1 (0.74)	0	1	
Candidal balanitis	4 (2.9)	0	4	
Nonvenereological GUDs				
Drug-induced GUDs	12 (8.8)	0	12	
Others	18 (13.3)	1	17	

HIV=Human immunodeficiency virus; GUDs=Genital ulcer diseases

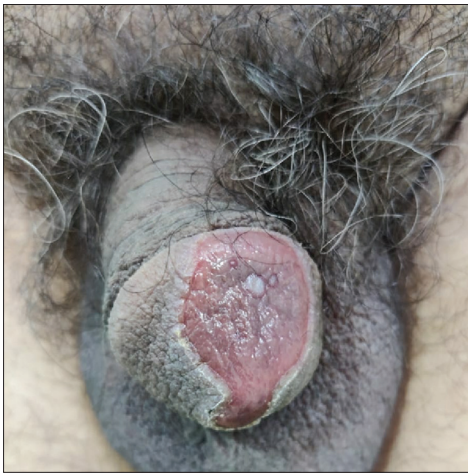


Figure 5: Genital ulcer in fixed drug reaction



Figure 6: Genital ulcer in pemphigus vulgaris



Figure 7: Genital ulcer in squamous cell carcinoma



Figure 8: Zoon's balanitis

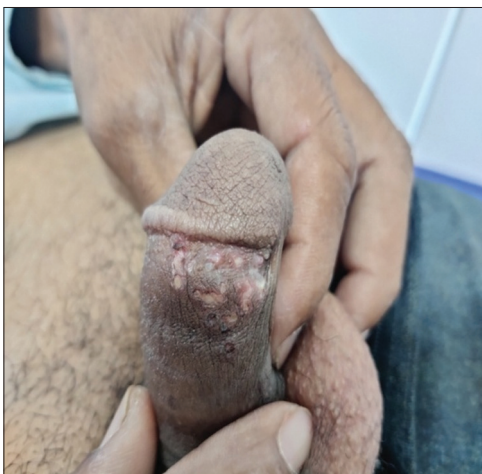


Figure 9: Herpes genitalis in male

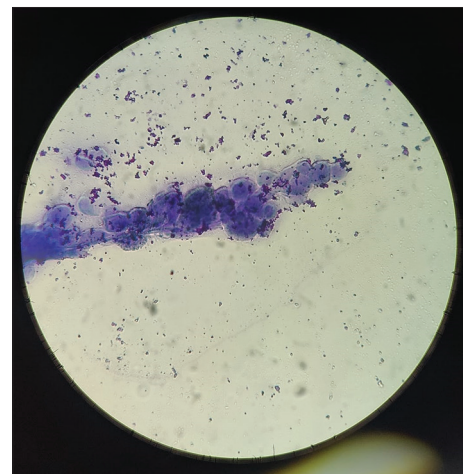


Figure 10: Acantholysis in Tzanck smear

homosexual category, and 1.09% ($n = 53$) of patients belonged to the bisexual class. 95.91% ($n = 658$) of patients were heterosexual, 2.77% ($n = 19$) were homosexual, and 1.31% ($n = 9$) were bisexual, as found in Narayanan.^[15] [Table 4]. There was no significant difference in HIV positivity due to sexual orientation ($P > 0.05$).

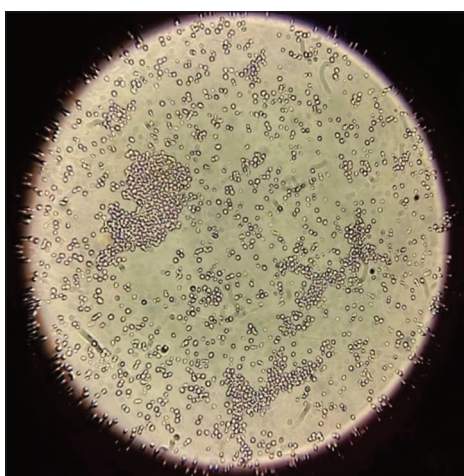
Homosexuality and bisexuality predisposed to a higher risk of acquiring/transmitting STDs. Recent evidence indicates a significant increase in the number of sexual partners and high-risk sexual practices in the population.

In this current study, 72% ($n = 97$) were married, 23% ($n = 31$) were unmarried, and 5% ($n = 7$) were

Table 4: Comparison of various studies with our study

Various studies Parameters	Narayan (January 1990–December 2000) ^[5]	Setia et al. (1994–2006) ^[12]	Muralidhar et al. (April 2010–March 2011) ^[13]	Nyati et al. (April 2012–March 2016) ^[14]	Our study (2021–2022)
Total number of patients	686	3417	90	4847	135
M/C age group	-	18–24	15–34	21–35	21–30
Gender					
Male	504 (73.5)	2985 (87.35)	60 (66.7)	1845 (38)	107 (79)
Female	182 (26.5)	406 (11.8)	30 (33.3)	3002 (62)	28 (21)
Marital status					
Married	378 (55.1)	1592 (46.6)	61 (67.8)	3411 (70.3)	97 (72)
Unmarried	308 (44.9)	1439 (42.11)	29 (32.2)	1373 (28.3)	31 (23)
Widowed/divorced	-	-	-	63 (1.3)	7 (5)
Sexual orientation					
Heterosexual	658 (95.91)	3061 (89.58)	89 (98.2)	4718 (97.3)	122 (90)
Homosexual	19 (2.77)	61 (1.78)	1 (2.2)	76 (1.6)	7 (5)
Bisexual	9 (1.31)	38 (1.11)	-	53 (1.09)	5 (3.7)
Sexually inactive	-	-	-	-	1 (0.74)
M/C GUD	Secondary syphilis 289 (57.3)	Chancroid 854 (25)	Herpes genitalis 71 (78.9)	Herpes genitalis 956 (51.8)	Herpes genitalis 80 (59)

M/C=Most common; GUD=Genital ulcer disease

**Figure 11: Potassium hydroxide smear of *Candida albicans***

widowed/divorced. Muralidhar et al.^[13] and Nyati et al.^[14] also showed that most cases were married patients, 67.8% and 70.3%, respectively. In our study, 70% ($n = 94$) of patients had a single sexual partner, 10.5% ($n = 14$) with multiple known partners, 10.5% ($n = 14$) had contact with female sex worker (FSW), 5.22% ($n = 7$) were man having sex with man (MSM), 3.73% ($n = 5$) had contact with FSW and MSM, and 1% ($n = 1$) was sexually inactive. Patients with a single sexual partner were also more in number, as observed by Nyati et al.,^[14] 65% ($n = 3155$), compared to patients with multiple sexual partners. All nine patients with HIV had multiple partners. This finding was statistically significant (<0.05).

Nyati et al.^[14] observed in the study period that 25.2% ($n = 1223$) of patients were using protection (condom), while in our study, only 16% ($n = 21$) were using contraception regularly. Unmarried, divorced, widowed, manual workers, and homosexual/bisexual preferences were found to be more reluctant to use the condom in other studies also. This much lower use of barrier contraception (condom) among study patients could be due to a lack of satisfaction, less comfort, and cultural practices.

In our study, we performed RPR and HIV tests on all 135 patients; 15% ($n = 20$) and 7% ($n = 9$) were found positive, respectively. In our study, nine patients had GUDs in the presence of HIV coinfection. In the study conducted by Muralidhar et al.,^[13] venereal disease research laboratory test and ELISA/rapid HIV tests were positive in 10% ($n = 9$) and 8.9% ($n = 8$), respectively.

Out of 135 cases of GUDs, the majority were venereological GUDs, 78% ($n = 105$), compared to nonvenereological GUDs, 22% ($n = 30$). Herpes genitalis 59% ($n = 80$) was found to be the most common among all GUDs in our observation. Muralidhar et al. (April 1, 2010–March 31, 2011)^[13] showed 78.9% ($n = 71$) of cases having herpes genitalis, Nyati et al. (April 2012– March 2016)^[14] showed 51.8% ($n = 956$) of cases, and Gupta et al. detected (2006–2015)^[20] 68.69% ($n = 79$) of patients having herpes genitalis. This result was similar to our study.

A study conducted by Narayanan (January 1900–December 2000),^[5] and Setia et al. (1994–2006),^[12] showed a result which contrasted with our study. Narayanan^[5] observed secondary syphilis 57.3% ($n = 289$), and Setia et al.^[12] found chancroid 25% ($n = 854$) as the most common GUDs in their study period. A reduction in bacterial GUDs and an increase in herpes cases have been reported from various studies during the last 15 years, while bacterial GUDs were more common in the last decade of 20th-century studies. In our study, we also included 15% ($n = 20$) syphilis, 8.8% ($n = 12$) drug-induced GUD, 5.9% ($n = 8$) traumatic GUDs, 4.4% ($n = 6$) pemphigus vulgaris, candidal balanitis 2.96% ($n = 4$), 1.5% ($n = 2$) Squamous cell carcinoma 0.7% ($n = 1$) Zoon's balanitis, 0.7% ($n = 1$) chancroid, and 0.7% ($n = 1$) Behcet's disease. The infection rate of HIV is higher in patients with venereological genital ulcers ($P < 0.05$).

Ulcerative sexually transmitted infections (STIs) are more prone to spread HIV compared to other STIs because there is a breach in the barrier function of skin and mucosa, thereby facilitating the entry of HIV into genital mucosa.

The main limitation of our study was the small sample size. Our other limitation was the unavailability of molecular diagnostic methods. We did not perform culture and real-time polymerase chain reaction tests in this study.

Conclusion

In our study, we concluded that among the GUDs herpes genitalis was most common. Furthermore, we observed a statistically significant association between the occurrence of herpes genitalis and HIV positivity.

Early age of sexual activity, multiple sexual partners, various sexual orientations, exposure to commercial sex workers, and unprotected sexual exposures are the risk factors for acquiring and transmitting GUDs. There was a significant association between HIV positivity and multiple partners, suggesting that there was more chance of GUDs and HIV infection in the case of multiple partners.

As the availability of baseline information on the epidemiology of STIs and associated risk behavior remains essential for designing, implementing, and monitoring successful targeted intervention, our study will also aid in the syndromic approach for the management of STIs.

This study aimed to provide an insight and overview of high-risk factors. Hence, it is highly recommended to increase efforts toward acknowledgment, safe sexual practices, periodic screening, and sexual health awareness programs in high-risk populations.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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