Original Article

Are we moving from symptomatic to asymptomatic syphilis: A retrospective analysis

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Abstract

Background: Syphilis remains a global health problem with recent reports of resurgence from various parts of the world. We undertook this study to analyze the current epidemiological and clinical trends of syphilis in our part of the country. **Aim and Objectives:** To analyze the changing trends in clinical presentation of syphilis and the current status of HIV/AIDS-syphilis co-infection in our area. **Materials and Methods:** This is a hospital-based retrospective analysis of records of sexually transmitted disease (STD) patients enrolled in "Suraksha clinic" in the department of Skin and VD at a Tertiary Care Hospital in North India. Patient records were analyzed from January 2018 to December 2021. The demographic, clinical, and serological profiles of patients were assessed to study the percentage of syphilis patients attending the STD clinic and their clinical presentations. **Results:** A total of 7153 patients were enrolled in the"Suraksha clinic" from January 2018 to December 2021, these included the venereal disease patients (3137) and nonvenereal disease patients (4016) who were registered for HIV and venereal disease research laboratory (VDRL) screening from the dermatology outpatient department. Out of 3137 sexually transmitted infection (STI) patients, 139 patients tested positive for VDRL. *Treponema pallidum* hemagglutination was found positive in 137 patients and negative in two patients. Hence, 137 patients were confirmed syphilis cases, constituting 4.36% of total STD cases in our STI clinic in 4 years. Out of 137 patients, 2 (1.45%) presented with primary chancre, 6 (4.37%) with lesions of secondary syphilis and 129 (94.16%) were found serologically reactive without any symptoms or clinical signs, i.e., in latent syphilis. Our records also showed 14 (10.21%) cases of HIV and syphilis co-infection. **Conclusion:** In our study, a remarkable rise in the number of patients in the latent syphilis stage is observed over primary and secondary syphilis stage. This signifies the persistence of syphilis in subclinical phase in the community and unfortunately, it goes unnoticed. These could be "warning signs" for changing disease pattern of syphilis in India and points toward hidden resurgence of syphilis as being reported in various parts of the world. To actively look for these "hidden cases," there is a need to strengthen "Suraksha clinics." VDRL testing should be mandatory along with routine testing in all patients visiting the hospital irrespective of their disease. We also propose for the central registration of syphilis patients on lines of HIV-infected patients' registry.

Key words: HIV, latent syphilis, syphilis

Introduction

Syphilis is an infectious venereal disease caused by the spirochete *Treponema pallidum*.[1] Routes of transmission described are unprotected sexual contact, from mother to fetus-in-utero, through blood product transfusion, and occasionally through breaks in the skin that come into contact with infectious lesions. If untreated, it progresses through four stages: primary, secondary, latent, and tertiary. Till date, there are few studies on the changing patterns of presentation of syphilis in our country. Although it is a well-known fact that nowadays primary and secondary stages of syphilis are less commonly seen which may be due to unchecked use of antibiotics and most of the syphilis cases are present in the latent stage but the documentation in literature is limited.

Materials and Methods

This is a hospital-based retrospective study in which data on syphilis was collected from January 2018 to December 2021 in "Suraksha clinic" in the Department of Skin and VD, at a tertiary care hospital in North

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India. The demographic profile, promiscuous behavior, clinical presentation, and serology of enrolled patients were noted. Diagnosis of syphilis was made based on clinical examination and serological investigations. Syphilis serology and HIV testing (as recommended by the National AIDS Control Organization) were done in the Microbiology department of the hospital as per protocol. Patients with reactive Venereal disease research laboratory (VDRL) were further confirmed by *T. pallidum* haemagglutination (TPHA). After retrieving the clinical records on syphilis, those who were both VDRL and TPHA reactive were segregated into primary, secondary, and latent stage of syphilis. Patients who were found to be VDRL reactive and TPHA negative, repeat VDRL testing was done and if was found reactive with no clinical signs of syphilis, it was considered a biologically false positive (BFP) reaction.

Inclusion criteria

Clinically and serologically diagnosed cases of syphilis as per records of the Suraksha clinic from January 2018 to December 2021.

Exclusion criteria

Cases with incomplete information.

Results

A total of 7153 patients were enrolled in the "Suraksha clinic" from January 2018 to December 2021. These included sexually transmitted disease (STD) patients and general outpatient department (OPD) patients who were registered for HIV and VDRL screening. Out of these 3137 cases were diagnosed with venereal diseases patients. Genital warts were the most common STD with 1076 (34.43%) patients, followed by vaginal discharge in 797 (25.40%) patients, herpes genitalis infection in 776 (24.73%), urethral discharge in 103 (3.28%) patients and 139 patients were found to be VDRL reactive [Figure 1]. TPHA was found positive in 137 patients and negative in two patients. Repeat VDRL test in TPHA negative patient was positive but patients did not show any signs and symptoms of syphilis, hence it was considered as BFP reaction. In total, 137 patients were confirmed with syphilis, constituting 4.36% of total sexually transmitted infection (STI) cases. The age group of the syphilis patients ranged from 17 to 79 years. Out of 137 syphilis cases, 99 patients were males and 38 were females (M: F: 2.6:1). VDRL titers of reactive patients ranged from 1:8 to 1:1024. Most of the male patients were laborers. Most of the females were housewives and were found positive on contact tracing of male patients. Nine male patients gave a history of homosexual behavior, 3 out of these were co-infected with HIV. BFP reaction was noted in two patients, constituting 1.43% of total VDRL reactive patients.

Out of 137 syphilis patients, 2 (1.45%) patients presented with primary chancre [Figure 2], 6 (4.37%) presented as secondary syphilis, and 129 (94.16%) patients presented in the latent stage of syphilis found VDRL and TPHA reactive on routine testing [Figure 3].

Out of 137 syphilis patients, 27 patients were found to have other concomitant STIs. Herpes genitalis was the most common concomitant STI, found in 13 cases (9.48%) followed by genital warts in 9 cases (6.56%) and molluscum contagiosum 5 cases (3.64%).

Out of a total of 3137 patients in STI clinic, 52 cases were found HIV positive. Forteen patients were found to have HIV and syphilis co-infection, accounting for 10.21% over total syphilis patients. Out of these 14 patients, none had primary chancre, 3 presented as secondary syphilis all with atypical mixed infections, one case was of Lues Maligna [Figure 4], the second case had concomitant herpes genitalis and molluscum contagiosum infection and the third case had florid condyloma acuminata with

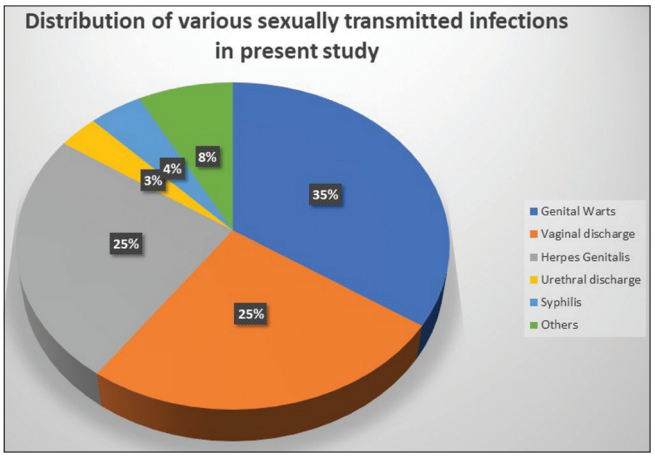

Figure 1: Distribution of sexually transmitted infections in "Suraksha Clinic"

Figure 2: Syphilitic primary chancre in a male patient

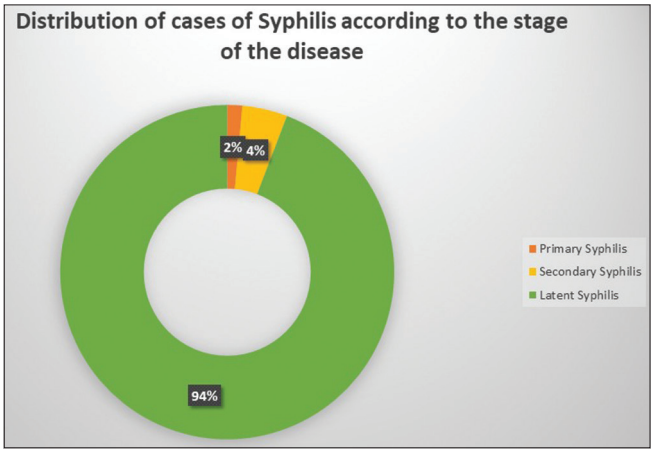

Figure 3: Distribution of patients according to the stage of the Syphilis

asymptomatic morbilliform rash [Figure 5]. Elven (78.57%) patients out of these 14 co-infected patients were found VDRL and HIV reactive on a routine investigation, i.e., in latent stage of syphilis.

Discussion

Syphilis and other STIs continue to be a major public health problem with a significant burden on the society, despite many health-care interventions and awareness created among the general public.[1] The co-infection with HIV has further complicated the existing scenario. There are various epidemiological studies demonstrating that STIs, including syphilis, are associated with an increased risk for HIV infection among both homosexuals and heterosexuals.[2-4] Recent studies points toward the resurgence of syphilis in various communities around the world as documented by dos Santos *et al.*,[5] Schmidt *et al.*[6] but Indian studies on syphilis prevalence are limited. We have compared our data with Indian studies of the past decade. Comparing the prevalence of syphilis as reported in various studies, the mean percentage of syphilis patients in STI clinic over 4 years in our study is 4.36%, which was reported as 7.36% by Jain *et al.*,[7] 11.82% by Sethi *et al.*[8] and 6.22% in by Nishal *et al.*[9] all in chronological order of the study period. Although the mean percentage of syphilis patients in STI clinics in India seems to be decreasing over a decade this could be due to increase in asymptomatic syphilis cases that are not reported to the medical facilities and it is probably masking the resurgence of syphilis as being reported in other parts of the world. While studying the annual percentage over 4 years, we found a dip in syphilis cases in our STI clinic in the year 2020, which might be due to covid pandemic. Barring covid lock-down time, the annual incidence of syphilis in our STI clinic showed a significant rise in percentage from 4.73% in 2018 to 5.27% in 2021, but the mean percentage of 4 years is 4.36% [Table 1].

As seen in other studies,[7-9] our study also showed male predominance (72.26%) and most of them were laborers. It might be attributed to the migratory nature of job, promiscuous behavior, and unprotected sexual practices that are common in them. The lower enrollment of females in STI clinic could be due to the higher social stigma of reporting to STI clinics. Thus, females were mainly detected as a part of partner management protocol or antenatal checkup. Majority of the cases were seen in the age group of 20–40 years and is mainly attributed to higher sexual activity clustering in this group as shown in [Table 2].

While studying the clinical presentation of syphilis and comparing our data with other studies [Table 3], we can see a dramatic decrease in primary syphilis, secondary syphilis, and increase in latent syphilis. Primary syphilis presented as the classical single indurated, painless genital chancre found in only 2 cases (1.45%) which is much less as compared to 21 cases (50%) in a study by Jain *et al.*[7] and 21 (13.08%) cases by Nishal *et al.*[9] There were 6 cases (4.37%) of secondary syphilis in our study, out of whom two patients were with asymptomatic maculopapular rash, one presented with lues maligna, one presented with condyloma lata, one had concomitant herpes genitalis and molluscum contagiosum infection and one presented with florid condyloma acuminata with asymptomatic morbilliform rash. Out of 6 cases of secondary syphilis, 3 were found to have concomitant HIV-syphilis co-infection. We observed a dramatic decrease in cases of secondary

Table 1: Annual distribution of syphilis cases

Year	Total STD cases	Number of syphilis cases	Percentage of syphilis cases	χ^2	*P*
2018	971	46	4.73	11.09	0.047
2019	1006	44	4.37		
2020	572	16	2.79		
2021	588	31	5.27		

STD=Sexually transmitted disease

Table 2: Year wise age and sex distribution of syphilis cases

Age group	<25 years		25-45 years		>45 years		Total
	Male	Female	Male	Female	Male	Female	
2018	3	2	25	10	4	2	46
2019	4	1	19	9	7	4	44
2020	2	1	10	2	1	0	16
2021	4	1	12	7	7	0	31

Table 3: Comparison with other studies

Stages of syphilis	Present study (2018-21), *n* (%)	Nischal *et al.*[9] (2008-12), *n* (%)	Jain *et al.*[7] (2005-2009), *n* (%)
Primary syphilis	2 (1.45)	21 (13.08)	21 (50)
Secondary syphilis	6 (4.37)	38 (41.76)	10 (24)
Latent syphilis	129 (94.16)	32 (35.16)	11 (26)
Total patients	137 (4.36)	91 (6.22)	105 (7.36)

Figure 4: Lues maligna (before and after treatment)

Figure 5: Florid Condyloma Acuminata in a patient with HIV-Syphilis co-infection

syphilis when compared to 24% cases of secondary syphilis in a study by Jain *et al*.[7] and 41.76% cases by Nishal *et al*.[9] Majority of the patients in our study were found on routine testing, i.e., in the latent stage of syphilis (129 cases, 94.16%). There is a surge in latent syphilis cases in our study as compared to 11 (26.19%) cases by Jain *et al*.,[7] and 32 (35.16%) cases by Nishal *et al*.[9] Latent cases were mostly diagnosed when patients were referred to STI clinic for other genital dermatoses or on screening investigations from general OPD or during blood donation camps or while applying for VISA and during ANC checkup. Other latent cases were detected as a part of partner management when their spouse/sex partners were detected with active disease signifying a lack of awareness as well as decreased use of barrier contraceptives. This increase in latent syphilis cases could be because of the long incubation period of syphilis, asymptomatic primary/secondary syphilis patients usually skip medical treatment, and due to inadvertent use of over-the-counter antibiotics that treat syphilis partially.

In our study, 10.21% of cases presented with HIV-syphilis co-infection. Eleven males and 3 females were found to be HIV and syphilis co-infected. Rising trends in HIV and syphilis co-infection were seen in our study as compared to 4.76% by Jain *et al*.,[7] 3.8% by Sethi *et al*.[8] and 8.79% by Nishal *et al*.[9] Out of 14 patients, three patients (21.42%) were in the stage of secondary syphilis and 11 patients with HIV and syphilis co-infection were found in latent stage accounting for 78.57% of patients, which is again alarming as in HIV-infected patients syphilis may go unnoticed if not tested serologically. Three cases of HIV-syphilis co-infection were homosexual males with a history of promiscuity. This indicates the need for strict screening protocols and behavioral modifications in this specific group.

Apart from syphilis, we also studied other STIs, genital warts were the most common STD in our clinic (34.30%), followed by vaginal discharge (25.40%) and herpes genitalis infection (24.73%). This is in comparison with a decade-back study by Jain *et al*.[7] where the most common STI was herpes genitalis (28%) followed by condyloma acuminata (20%). However, similar to a relatively recent study, by Nishal *et al*.,[9] where genital warts (35.15%) were the most common STI followed by herpes genitalis (33.72%). The reason for increased genital warts could be due to the long incubation period, autoinoculation, multiple seedlings, and asymptomatic nature, hence ignored by patients as compared to painful herpes genitalis which is readily treated and its transmission aborted under syndromic management of STI's.

Conclusion

Current epidemiological trends as per our study show a significant increase in latent syphilis cases which were mainly detected on screening investigations during blood donation camp or while the patient is undergoing medical examination for VISA application or some other purposes. Although the mean percentage of syphilis patients in our STD clinic over 4 years is less as compared to previous studies, this cannot be commented as "decreasing trends of syphilis," as completely asymptomatic latent syphilis cases are not reported. This could also be due to limited epidemiological documentation of syphilis cases, attributed to the stigma attached to STIs, poor attendance in STD clinics, and lack of a common registry portal. This trend of increase in latent syphilis cases is actually worrying, given the fact that these active but asymptomatic syphilis cases are spreading the disease in community without being noticed. And if actively searched we might see a surge in syphilis in our country as seen in other parts of the world. Furthermore, approximately 14% of untreated latent syphilis cases end up with tertiary syphilis sequelae with neurological and cardio-vascular complications, adding morbidity to the already burdened health-care facilities in our country.

Thus, strong measures should be taken to promote active surveillance of syphilis cases through increased testing and treatment strategies in resource-limited setting. Frequent community check-ups on war front are required to detect maximum number of serologically active syphilis cases and their timely treatment before transmission of syphilis to a healthy person. Appropriate measures should be proposed to form a consolidated central registry system for better epidemiological understanding of syphilis. Emphasis should be put on over promotion of healthcare-seeking behavior among high-risk populations, especially woman and methylsulfonylmethane for frequent screening, treating patients with syphilis quickly, identifying and treating sexual contacts, and re-screening.

Limitations

This is a single-center, retrospective study over a limited period. Epidemiological studies of longer duration on serological syphilis are required to bring out the exact data on the prevalence of syphilis in our country.

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Conflicts of interest

There are no conflicts of interest.

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