



EMERGING TREND OF SYPHILIS IN STD CLINIC ATTENDEES IN A TERTIARY CARE HOSPITAL IN NORTH-EAST INDIA.

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Abstract:

Background: Syphilis is a sexually transmitted disease (STD), caused by *Treponema pallidum* subsp. *pallidum*. Increasing trend of syphilis infection has been observed in North-East India in recent years.

Aim: To study the prevalence of syphilis infection among the STD clinic attendees.

Settings and Design: This retrospective study was conducted in Gauhati Medical College & Hospital, a tertiary care hospital from April 2020 to September 2021 considering the OPD attendees of STD clinic, Department of Dermatology.

Material and Method: Blood samples received from STD clinic attendees were analysed for the study. The serum samples were subjected to qualitative RPR test followed by quantitative RPR and TPHA using standard procedure. Samples which were reactive by both quantitative RPR and TPHA were considered as seropositive for syphilis.

Statistical Analysis: Carried out with Microsoft Office Excel.

Results: The seroprevalence of syphilis was found to be 10.61%. Higher seroprevalence was noted among the sexually active age groups (21-40 yrs). Males showed higher seroprevalence indicating high risk behaviour (MSM) and unsafe sexual practices.

Conclusion: Prevalence of syphilis is quite high amongst the STI clinic attendees in our hospital which can be reduced by behaviour modification, promoting safe sexual practices, enhanced case detection, treatment and follow up.

Key Words: RPR, Syphilis, Seroprevalence, STI clinic, TPHA.

Introduction

Sexually transmitted diseases (STDs) are widespread in the developing countries and constitute a major threat in India.^[1] According to a recent global health-sector strategy on sexually transmitted infections for the years (2016–2021) maneuvered by The World Health Organization's (WHO's), 90% reductions in the incidence of *Treponema pallidum* (syphilis) and *Neisseria gonorrhoeae* (gonorrhoea) infections between 2018 and 2030 has been targeted.

The most serious public health problems in the WHO South-East Asia Region have been attributed to sexually transmitted infections with considerable associated morbidity, mortality, disability and adverse pregnancy outcomes.^[2,3,4]

Syphilis is a sexually transmitted disease caused by *Treponema pallidum* mainly through sexual intercourse and also by other modes such as blood transfusion and Mother-to-Child transmission. The World Health Organisation (WHO) estimates that there are 6 million new infections every year globally.^[5] Syphilis is a serious public health problem because it can increase the risk of HIV acquisition by three-fold or more. The signs and symptoms of syphilis vary depending upon which of the four stages it presents (Primary, Secondary, latent and tertiary). The primary stage classically presents with a single chancre (a firm, painless, non-itchy skin ulceration usually between 1 cm and 2 cm in diameter) though there may be multiple sores. In secondary syphilis, a diffuse rash occurs, which frequently involves the palms of the hands and soles of the feet. There may also be sores in the mouth or vagina. In latent syphilis, which can last for years, there are few or no symptoms. In tertiary syphilis, there are gummas (soft, non-cancerous growths), neurological problems or heart symptoms. Syphilis has been known as “the greater imitator” as it may cause symptoms similar to many other diseases. Diagnosis is usually made by blood tests; the bacteria can also be detected using dark field microscopy.

The risk of sexual transmission of syphilis can be reduced by using a latex or polyurethane condom. Syphilis can be effectively treated with antibiotics. The preferred antibiotics for most cases are benzathine benzylpenicillin injected intramuscularly. In those with neurosyphilis, intravenous benzylpenicillin or ceftriaxone is recommended. During treatment people may develop fever, headache and muscle pains, and a reaction known as Jarisch-Herxheimer.

In 2015, about 45.4 million people were infected with syphilis, with six million new cases. During 2015, it caused about 107,000 deaths, down from 202,000 in 1990. Occurrence of syphilis decreased dramatically with the availability of penicillin in the 1940s. But rates of infection have again increased since the turn of the millennium in many countries, often in combination with human immunodeficiency virus (HIV). This is believed to be partly due to increase promiscuity, prostitution, decreasing use of condom and unsafe sexual practices among men who have sex with men. Syphilis is a serious public health problem because it can increase the risk of HIV acquisition by three-fold or more.

The objective of the present study was to find out the seroprevalence of syphilis in patients attending STI clinic in our region as well as to study the socio-demographic characteristics associated with it.

Materials and Methods

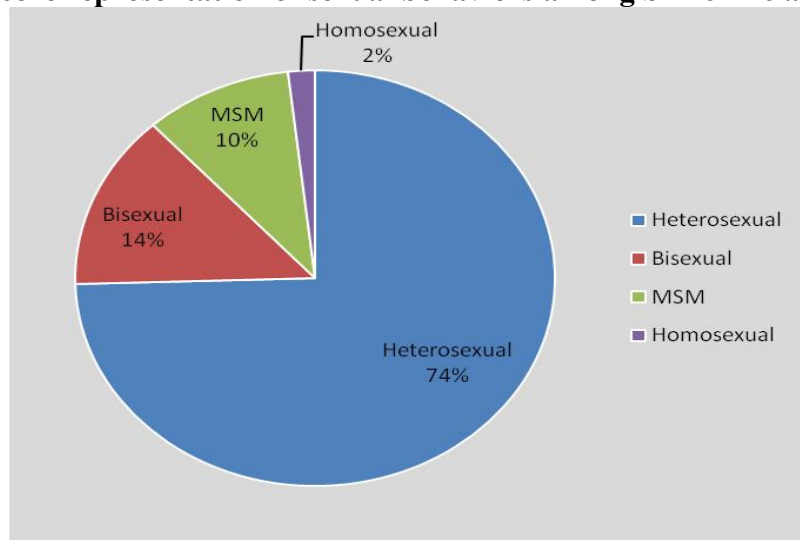
This study was conducted in the Department of Microbiology, Gauhati Medical College & Hospital, which is a tertiary care teaching hospital in North-East India after obtaining ethical clearance certificate from Institutional Ethics Committee, Gauhati Medical College & hospitals vide number MC/190. It is a prospective hospital-based study done over a period of one year from April 2020 to September 2021. The study population consisted of all patients with high risk of syphilis or with clinical suspicion of syphilis who had attended the STI clinic as part of routine screening for syphilis. Thus, the study population included HIV seropositive patients attending ART centre, patients referred from Integrated Counselling and Testing Centre (ICTC), intra venous drug users (IVDU), STI clinic attendees without HIV and patients from other wards or OPDs. Blood Samples were collected from all the subjects in the study population aseptically. All the serum samples were initially tested by qualitative Rapid Plasma Reagin (RPR) test using standard procedures and the reactive samples were further tested by quantitative RPR and a specific treponemal test, *Treponema Pallidum* Haemagglutination Assay (TPHA Kit BIO-RAD™, France) for detection of antibodies to *Treponoma pallidum*. Samples which were reactive by both quantitative RPR and TPHA were considered as seropositive for Syphilis. The quantitative titers of the patients having positive serology were tabulated accordingly. The sociodemographic characteristics were obtained using a predesigned questionnaire. Statistical analysis including charts was prepared using the Microsoft Excel.

Results

Demographic characteristics of the patients:

Out of a total of 1036 STI attendees, 403 were males and 633 were females. While considering the sexual behavior of patients included in this study the major section belongs to heterosexual (74%) followed by bisexual (14%), Man having sex with men (MSM) 10% and homosexual (2%) depicted in Fig.1.

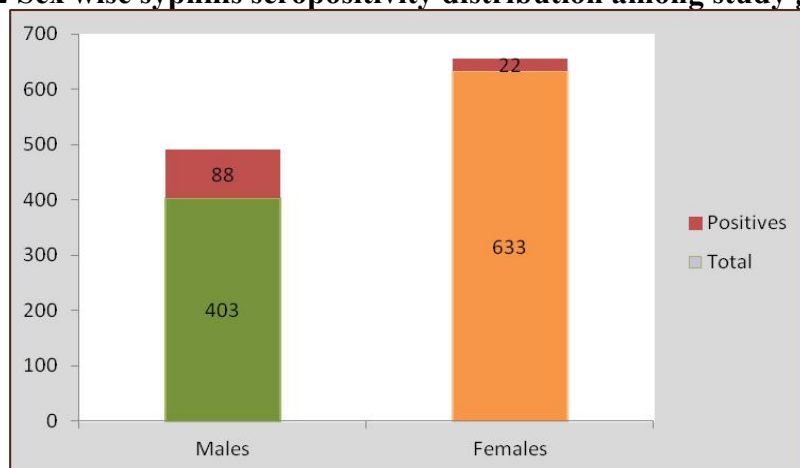
Fig1. Score representation of sexual behaviors among STI clinic attendees



Data are presented in percentage (%) with a total sample size n=1036.

Among the 1036 samples tested for syphilis, 110 samples were reactive by both quantitative RPR test and TPHA. The overall seroprevalence in this study was found to be 10.61%. Seropositivity for syphilis was found in 88 males (21.84%) and 22 females (3.48%). Represented in Fig.2.

Fig.2 Sex wise syphilis seropositivity distribution among study group



The male to female ratio was reported to be 4:1. The age wise distribution of Syphilis reactive cases and literacy status of the RPR positive patients are depicted in Table 1 and Table 2 respectively.

Table 1. Distribution of seropositive cases of syphilis according to age

Age Group	No. of Positive Cases	Percentage
0 – 10	1	0.9%
11 – 20	5	4.54%
21 – 30	61	55.45%
31 – 40	35	31.81%
41 – 50	8	7.27%
51 and above	0	0%

Table 2. Literacy status of the patients

Literacy level	No. of positive cases	Percentage
Graduate	17	15.45%
12 th pass	49	44.54%
10 th pass	24	21.81%
< 10 th pass	13	11.81%
Illiterate	6	5.45%
Others	1	0.90%

Among the different age groups, 104 cases were found positive in the 20 to 49 years age group (94.54%) while 5 cases (4.54%) were positive in (10-20) year age group considering both sexes. One positive case was a newborn which was 2 days old (case of mother to child transmission). No seropositive case of syphilis was found above 50 years of age. Majority of syphilis seropositivity was noted in the sexually active age group. Among the patients positive for syphilis, highest seroprevalence of males (23.64%) was observed in the 25 to 29 age groups while among the females, the seroprevalence was 10% in the same age group. Seropositivity of syphilis infection among different age groups is represented in Table 3.

Table 3. Showing the seropositivity of syphilis infection among different age groups

Age Group	Total No. Tested	Male		Female		Total No. Positive (%)
In Years		No. Tested	No. Positive (%)	No. Tested	No. Positive (%)	110
0-4	9	3	0	6	1 (0.9)	1
15-19	41	14	1(0.91)	27	2(1.82)	3
20-24	225	86	14(12.73)	139	2(1.82)	16
25-29	258	124	26 (23.64)	134	11(10)	37
30-34	194	98	23(20.91)	96	3(2.73)	26
35-39	141	75	14(12.73)	76	4(3.64)	18
40-44	81	36	2 (1.82)	45	0	2
45-49	67	23	5(4.55)	44	0	5
50-54	36	24	2(1.82)	12	0	2

Most of the seropositive cases 64 (58.18%) were STI clinic attendees, 11 (10%) cases referred to the STI clinic from Integrated Counseling and Testing Centre (ICTC), and 8 (7.27%) HIV seropositive cases were referred from the Anti-Retroviral treatment (ART) centre. The other cases were referred from the Antenatal Clinics 5(4.54%), Blood Bank 1(0.91%), Others in 3(2.73%), General ward 1(0.91%), Gastro-OPD 2(1.81%) people who had come to the STI clinic for testing by themselves 12 (10.9%) or referred by NGO 3 (2.73%).

The patients reported to the clinics presented with symptoms including Urethral discharge, Genital Ulcer disease (GUD) non-herpetic, Vaginal cervical discharge, No-rectal discharge, Scrotal Swelling, Genital Warts, Lower Abdominal Pain, Presumptive treatment and Asymptomatic

patients. Co-infection was observed with cases of Genital Ulcer disease (GUD), Inguinal Bubo, Genital Scabies, Genital Molluscum, Genital Pediculosis.

Among the 110 patients positive for syphilis, majority of the patients 24 (21.82%) had genital ulcers, followed by genital warts in 23 (20.91%), ulcers in 17(15.45%), genital candidiasis in 11(10%), vaginal discharge in 5(4.55%), genital herpes in 4 (3.64%), chancroid in 2 (1.82%), urethral discharge in 1(0.91%) and another 23(20.91%) patients were asymptomatic. Detailed clinical symptoms among syphilis patients are depicted in Table 4.

Table 4. Symptoms present in the syphilis patients

Symptoms	No. of cases	Percentage
Urethral discharge	1	0.91
Painless Ulcer/Ulcer	17	15.45
Genital Ulcer	24	21.82
Vaginal discharge	5	4.55
Genital Candidiasis	11	10
Chancroid	2	1.82
Genital Warts	23	20.91
Genital Herpes	4	3.64
Asymptomatic	23	20.91

Syphilis and HIV co-infection

Out of a total of 110 cases of syphilis, HIV co-infection was found in 23 cases (20.9%). The co-infection rate of HIV and syphilis was 30.43% (7/23) in men who have sex with men (MSM). The sexual behaviour of the seropositive cases of syphilis has been shown in Figure 1.

Quantitative analysis of the patients with HIV

A comparison of the quantitative titers of the RPR values was made among the positive for syphilis and HIV co-infected patients and presented in Table 5. Out of the 21 syphilis patients co-infected with HIV, 6 (28.57%) patients reported titers of R1:2, 3 patients (14.28%) reported titers of R1:4, 6 (28.57%) patients presented with high titers of R1:64 while of the remaining 6 patients, each of the 2 (9.52%) patients reported each with titers of R1:8, R1:16 and R1:32 respectively (Table 5). Majority of the patients 8 (38.09%) were reported from the Anti Retroviral Treatment (ART) clinics among which 4 (50%) patients had high titer of R1:64, 2 (25%) patients had titer of R1:4, while the rest 2(25%) patients had RPR titer of R1:4 and R1:32 each, respectively. Secondly, 7 patients (33.33%) were reported from the STI clinics where each of the 28.57% patients had titers of R1:2 and R1:64 respectively, the remaining each of the 14.28% patient had titers of R1:4, R1:8 and R1:32 respectively. In the ICTC clinics, 4 (19.04 %) patients were reported with 3 (75%) patients having low RPR titers of R1:2 while a single patient had titer of R1:8. Further, 2 (9.52%) patients reporting to the hospital on their own had a titer of R1:16.

Table 5. Comparison of quantitative titers of RPR among the patients having syphilis and HIV co-infection(n=21)

Reactive RPR Titer	STI (n)	ART(n)	ICTC(n)	SELF(n)	Total (%)
R1:2	2	1	3	0	6 (28.57%)
R1:4	1	2	0	0	3 (14.28%)
R1:8	1	0	1	0	2 (9.52%)
R1:16	0	0	0	2	2 (9.52%)
R1:32	1	1	0	0	2 (9.52%)
R1:64	2	4	0	0	6 (28.57%)
Total	7(33.33%)	8(38.09 %)	4(19.04 %)	2 (9.52%)	21

Among the 110 patients positive for syphilis, a comparison of the RPR titer values with low RPR titers below 1:8 and high RPR titers above 1:8 was made among the patients in the STI clinics, Antenatal clinics (ANC), ICTC clinics and patients reporting on their own reported in the Table 6.

In the STI clinic, 38 (54.28%) patients were reported out of the 70 patients with syphilis having high RPR titer greater than 1:8, while among the remaining 40 patients with low RPR titer less than equal to 1:8, 26 (65%) had low RPR titers levels less than 1:8.

In the ART clinic, remarkably, 5 (12.5%) out of the 40 syphilis positive patients reported with RPR titer levels less than 1:8, while only 3(4.28%) out of the 70 patients had higher RPR titers greater than 1:8, even though it was not significant.

In the ICTC clinics, it was observed that the 11(15.71%) patients had high RPR titers greater than 1:8 which was significantly higher ($p < 0.01$) compared to none of the patients with a lower titer less than 1:8 (Table 6).

Table 6: Distribution of quantitative titers of RPR in the patients having syphilis in the STI, ANC, ART, ICTC clinic and SELF attendees

Groups	RPR >1:8(N=70)	RPR <1:8 (N=40)	P value
STI Clinic	38	26	0.14
ART	3	5	0.06
ICTC	11	0	$P < 0.01$
SELF	9	3	0.20
ANC	4	1	0.24
GOPD	1	1	-
NGO	1	2	-
BLOOD BANK	0	1	-
GEN	0	1	-
OTHER	3	0	-

Abbreviation: STI- Sexually Transmitted Infection, ART-Anti Retroviral Treatment, ICTC-Integrated Counselling and Testing Centre for HIV, ANC-Anti Natal Clinic, GOPD-Gynaecology Outpatient Department, NGO-Non-Government Organization, GEN-General.

In the ANC clinic, 4 (5.71%) out of the 70 syphilis positive patients reported with higher RPR titers above 1:8 while only 1(2.5%) patient out of 40 syphilis positive patients with low RPR titers less than 1:8. No other significant numbers of patients with high or low RPR titers were reported from the Gastric OPD, Blood Bank, General Ward, NGO and other clinics in the hospital.

Discussion:

The global epidemiological profile of STDs has shifted over time, with viral infection surpassing bacterial ones due to change in sexual practices and HIV epidemic.^[6] However Syphilis prevalence has remained relatively stable that can be supported by the recent studies from India and Western countries.^[7,8] During the last five years, an increasing trend of syphilis was observed. The increasing incidence of Syphilis is also a worrying factor. We have also studied the incidence of syphilis. This warrants further study to evaluate change in infection titer or frequency of re infection in patients co-infected with HIV. In the current study, most of the patients having syphilis were males with the male to female ratio being 4:1, with a higher seropositivity being observed in males compared to the females. This finding is accordance with recent studies from North India where the male to female ratio was reported to be 6:1.^[9] This might be due to the higher social stigma in females of reporting to the STI clinics. But on the contrary, previous studies conducted in India reported equal proportions of transmission of the infection in both the genders.^[10] Since only the suspected patients or high-risk patients or patients attending STI clinic are usually tested for syphilis serology a higher seroprevalence of syphilis in males can be observed whereas in ANC clinics all the females are

routinely screened for syphilis and therefore the number of female patients is more compared to the male patients. A similar observation was made in a study from a tertiary care center in India.^[11]

In several countries, the co-infection rates of syphilis and HIV have been displaying a worrisome trend, with outbreaks in men who have sex with men having rates of 20%- 73%.^[12] In India, the varying co-infection rates of syphilis and HIV have been described.^[13] Similarly, in our current study, co-infection rate of syphilis and HIV was observed in 20.9% (23/110) patients among which 30.43% (7/23) of the cases were men who have sex with men. In USA, in 2016 men having sex with men (MSM) accounted for the majority (58.1%) of reported primary and secondary Syphilis cases.^[14] Tao et al. reported a higher seroprevalence of Syphilis 45% among female sex workers in China.^[15] Despite several studies on the occurrence of syphilis facilitating acquisition of HIV being reported, but till date there is no clear evidence of surge in the spread of the HIV infection.^[16,17]

The majority of patients in our study belonged to the age group 20-29 year which may be due to the increased sexual activity with higher number of sexual partners and multiple relationships in this age group. A similar pattern was reported in a study conducted in Puducherry.^[18]

Majority of patients having syphilis in our study 51.81% (57/110) were unmarried with most of the patients having sexual history of multiple partners. A smaller proportion 24.54% (27/110) of males and female patients in our study were married and most of them gave a history of risky sexual behaviour. Similar results were reported in a study from Ahmedabad.^[19] In our current study, majority of patients 81 (73.64%) having syphilis reported with heterosexual behaviour while 10% (11/110) patients belonged to the category of men who have sex with men (MSM) and 2 /110 which represent homosexual behaviour among the patients. Another 13.63% (15/110) patients with syphilis reported with bisexual behaviour which reveals a varying pattern in the sexual behaviour among the patient pool and which needs to be monitored carefully.

Previously in a study of consecutive five years from 2004-2008, it was reported that Syphilis was prevalent in the STD patients in about 8.2% patients (103/674) with 8.9% prevalence among women and 7.7% among men.^[10] The data also showed highest seroprevalence among the 20-24 age group (16.3%), and the lowest seroprevalence in the 45-49 age group (3.3%). But in the current study the prevalence of syphilis was found to be as 10.61%. The study is first of its kind in North East India and highlights the prevalence of syphilis in a huge patient pool. In another study carried out in North India in about 28,920 serum samples, a rising trend in pregnant women, drug users and patients from wards/out-patient departments were observed, while there was a statistically significant rise in the prevalence of syphilis in HIV-positive individuals.^[20] In a contrasting study from Southern India, the authors reported a declining trend in the prevalence of Syphilis among 14,639 samples over a two-year period in a tertiary care hospital.^[21] Our study reports a comparable declining trend in the Syphilis prevalence rate in our hospital set up.

In India, various studies have reported Syphilis seropositivity among STD clinic attendees ranging from 1.89% to 11.7%.^[22-25] The seroprevalence of syphilis in antenatal groups has been reported to be 0.84% to 0.98% in several Indian studies.^[26,27] On the contrary, we observed a seropositivity rate of 4.54% (5/110) among the syphilis positive patients reporting from the antenatal clinics.

In our study, the major common symptom among majority of the patients in our study having syphilis was genital ulcers which constituted of 21.82%. In a study conducted in general population among 2456 adults from different states from North India, the prevalence of syphilis was found to be 1.7%,^[28] while in the current study the prevalence was reported to be 10% which depicts a higher seroprevalence in the North Eastern part of the country.

Owing to results from several studies, CSF examinations have been recommended for HIV-infected patients with a RPR titer $R \geq 1:32$, irrespective of the syphilis stage, or for those with early-stage infection and a CD4 cell count ≤ 350 cells/mL, regardless of titer and hence RPR titers of the co-infected patients of HIV and syphilis were noted in the current study.^[29] In our current study, 70 (63.63%) patients reported with high RPR titers greater than R1:8 compared to 40 (36.36%) patients with low RPR titer less than R1:8. In the ICTC clinics the RPR titers greater than R1:8 in 11(15.71%) patients was significantly higher ($p < 0.01$) compared to none of the patients with a lower titer less than R1:8. This could be attributed to the co-infection of patients with HIV with a

positive syphilis serology reported to the ICTC clinics. This is one of the first studies where the titer of patients with syphilis is reported from North-Eastern India.

As reported in previous studies regarding prevention of syphilis, public health efforts targeting Internet users are useful measures in increasing alertness about syphilis.^[30] A routine screening and promotion of safe sex is highly recommended among the sex workers as well as in the general population. A timely diagnosis of these co-infections can lessen the downstream offset rapid disease progression, encourage cure and, importantly reduce transmission to partners and children which would cumulatively decelerate co-infection epidemics.

Our study had several limitations. Since our current study was a hospital-based study, the results may likely be different from population-based community studies. Secondly, we were unable to evaluate several parameters like risk evaluation of particular groups such as men who have sex with men and demarcate rural and urban population etc. Finally, the study was conducted over a short period of one year. More epidemiological data could be generated from long term studies with larger number of patients. Nevertheless, findings of this study would yield more data which would help us in understanding the disease trend in this part of India.

Conclusion

We observed a falling trend of syphilis in STD clinic attendees while a rising trend was observed in HIV-seropositive individuals, IVDUs, pregnant women, and patients from other wards and OPDs. The results may not reflect the true prevalence of syphilis in the community as this was a hospital-based study. Also, many patients with STDs approach private practitioners, and patients coming to our tertiary care center represent just the tip of this iceberg. Nevertheless, the observation of increasing trends in certain vulnerable subpopulation such as HIV patients, IVDUs, and pregnant females' calls for continued and sustained efforts for case detection, treatment, and other preventive measures to contain the disease.

Acknowledgement

The authors sincerely acknowledge the Assam State AIDS Control Society (ASACS) and National AIDS Control Organization (NACO) for supporting us to carry out the study. We also acknowledge Mr. Baharul Islam, Laboratory Technician, Regional STI Training Research and Reference laboratory (RSTRRL), Gauhati Medical College & Hospital for his extended support for conducting serological tests during the study.

Conflict of interest: None to declare.

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