

Syphilis in the era of re-emergence: A 6-year retrospective study from a tertiary care center in South India

Palanisamy Jeevanandham, Betsy Ambooken, Neelakandhan Asokan, Sarin Abdul Salam, Renu Venugopal
Department of Dermatology, Venereology and Leprosy, Government Medical College, Thrissur, Kerala, India

Address for correspondence:

Dr. Sarin Abdul Salam, House No. 19/204-7, Sruthi, P and T Quarters Road, Poothole P. O., Thrissur - 680 004, Kerala, India.
E-mail: asarin14@gmail.com

Abstract

Background: During the last several years, we have observed a rise in the number of patients with syphilis in our center. **Aims:** To find out the trends in the presentation of syphilis to our clinic over a 6-year period and to analyze the clinicoepidemiological features of those patients. **Settings and Design:** A retrospective chart review. **Subjects and Methods:** We analyzed the case records of all cases of syphilis registered in our sexually transmitted infection (STI) clinic from October 1, 2012, to September 30, 2018. Syphilis was diagnosed based on clinical or serological evidence. We also evaluated these patients for any concomitant STI, including hepatitis B, hepatitis C, and HIV. **Statistical Analysis Used:** The data were analyzed using SPSS software (version 20). Chi-square test was done for comparing categorical data, and $P < 0.05$ was considered statistically significant. **Results:** During the study period, 215 patients with STI attended our clinic. Of these, 66 (31%) patients had acquired syphilis. Among them, 3 (4.5%) had primary syphilis, 23 (34.8%) had secondary syphilis, and 40 (60.6%) had latent syphilis. Fifteen (22.7%) patients had concomitant HIV infection. A statistically significant rise in the number of cases of syphilis compared with other STIs was noted in the latter half of the study period ($P = 0.001$). Among the 50 males with acquired syphilis, 29 (58%) were men having sex with men (MSM), including 19 bisexual persons. Among the five antenatal cases, two were detected very late in pregnancy. **Conclusions:** We observed a marked increase in the number of cases of syphilis during the latter half of the study period. Primary and secondary syphilis were more frequent among MSM, suggesting a need to strengthen targeted intervention programs among them. More rigorous antenatal screening is necessary to prevent congenital syphilis.

Key words: Antenatal, men having sex with men, re-emergence, syphilis

Introduction

Worldwide, there was a marked rise in the incidence of viral sexually transmitted infections (STIs), including HIV, during the late 1990s, and a relative fall in the incidence of bacterial STIs like syphilis, chancroid, and gonorrhea.^[1,2] Following that, in the first two decades of this century, an increasing trend in the incidence of syphilis was observed. Re-emergence of syphilis in HIV positives was reported by Pialoux *et al.* in Europe and the United States in 2008 and Shah *et al.* in India in 2015.^[3,4] Muldoon and Mulcahy noticed a rising trend of syphilis in Ireland from 2007 to 2009.^[5] There has also been changes in sexual practices, with more people, especially men who have sex with men (MSM), engaging in penoanal and orogenital contacts.^[6]

Recently, in our tertiary care hospital, we have been observing a steady rise in the number of patients with syphilis, especially secondary and primary syphilis. Hence,

we decided to undertake a 6-year retrospective study on the trends in the frequency of presentation of patients with syphilis in our STI clinic and their clinicoepidemiological profile.

Subjects and Methods

After obtaining permission from the institutional ethics committee, a retrospective chart review of all cases who attended the STI clinic from October 1, 2012, to September 30, 2018, was done. Those cases diagnosed and treated as syphilis were included in the analysis. Demographic details of age, sex, occupation, and marital status, history of premarital or extramarital sexual contact, sexual preference (homo/hetero/bisexual), history of orogenital/penovaginal, penoanal contact, whether an active or passive partner in case of MSM, duration of symptoms,

This is an open access journal, and articles are distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 4.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as appropriate credit is given and the new creations are licensed under the identical terms.

For reprints contact: WKHLRPMedknow_reprints@wolterskluwer.com

How to cite this article: Jeevanandham P, Ambooken B, Asokan N, Salam SA, Venugopal R. Syphilis in the era of re-emergence: A 6-year retrospective study from a tertiary care center in South India. *Indian J Sex Transm Dis* 2022;43:165-9.

Submitted: 13-Dec-2021
Accepted: 13-May-2022

Revised: 28-Apr-2022
Published: 01-Aug-2022

Access this article online

Quick Response Code:



Website:

www.ijstd.org

DOI:

10.4103/ijstd.ijstd_109_21

symptoms of all STIs including HIV were noted. The characteristics of genital ulcer, skin rash, any other mucosal lesions, lymphadenopathy, any other concomitant STI and details of treatment received were collected.

Men/women who reported having sex only with the opposite gender were considered as heterosexuals. Men who reported having sex with the same gender were considered as MSM. Men/women who reported having sex with partners of both the genders were considered as bisexuals.

A clinical diagnosis of primary syphilis was suspected in patients who had a painless indurated genital ulcer. In all genital ulcers, dark ground microscopy was done to demonstrate treponemes and Gram stain for *Haemophilus ducreyi* bacillus. If herpes was suspected, Tzanck smear was done for multinucleated epithelial giant cells. According to the latest Sexually Transmitted Diseases Treatment Guidelines by the Centers for Disease Control and Prevention (CDC), a nontreponemal test (rapid plasma reagin [RPR] test or venereal disease research laboratory [VDRL] test) and a treponemal test (treponema pallidum hemagglutination [TPHA] test) were done for the presumptive diagnosis of syphilis.^[7]

A clinical diagnosis of secondary syphilis was suspected in patients with asymptomatic macular or papular skin rash, mucosal lesions on the oral, genital, or anal mucosa, and generalized lymphadenopathy with or without systemic symptoms. Dark ground microscopy was done to demonstrate treponemes from most lesions on the skin or mucosal lesions. Diagnosis of secondary syphilis was further confirmed by serological tests such as RPR or VDRL in dilution and TPHA.

A diagnosis of latent syphilis was made if nonspecific tests such as RPR or VDRL and specific tests such as TPHA were positive in patients with no clinical features of syphilis. A thorough clinical evaluation for features of cardiovascular, ocular, and neurosyphilis was done in all cases before making a diagnosis of latent syphilis. Cases within 1 year of acquiring syphilis were classified as early latent and those of more than 1-year duration as late latent syphilis. Cases with high-risk sexual behavior or having a partner diagnosed with syphilis reporting negative nontreponemal tests but positive treponemal tests were also diagnosed as latent syphilis if they presented with no documented treatment for syphilis. Patients, whose exact duration of disease was unknown, were designated as latent syphilis of unknown duration and were grouped under late latent syphilis. A diagnosis of congenital syphilis was made as per the CDC guidelines (MMWR 2015) and as per the national strategy and operational guidelines toward the elimination of congenital syphilis.^[7,8] Serological tests for HIV, hepatitis B, and hepatitis C were done for all patients.

The data were entered into MS Excel and analyzed using SPSS software (version 20, IBM, USA). Chi-square test was done for comparing categorical data, and $P < 0.05$ was considered statistically significant.

Results

During the 6-year study period, 215 patients attended the STI clinic of our institution. Of these, 66 (31%) patients were diagnosed as acquired syphilis. To analyze the trend in recent years, we divided the study period into two equal halves, the first half from October 1, 2012, to September 30, 2015, and the second from October 1, 2015, to September 30, 2018. Of the 75 patients

with STIs attending our clinic in the first half of the study, 11 (14.7%) had acquired syphilis compared to 55 (39.3%) among 140 patients who attended in the second half ($P = 0.001$) [Table 1]. Figure 1 shows the number of cases in each stage of syphilis across the study period. Age of patients with acquired syphilis ranged from 18 to 62 years with the majority ($n = 29$, 43.9%) belonging to 21–30 years [Table 2]. Twenty-six (52%)

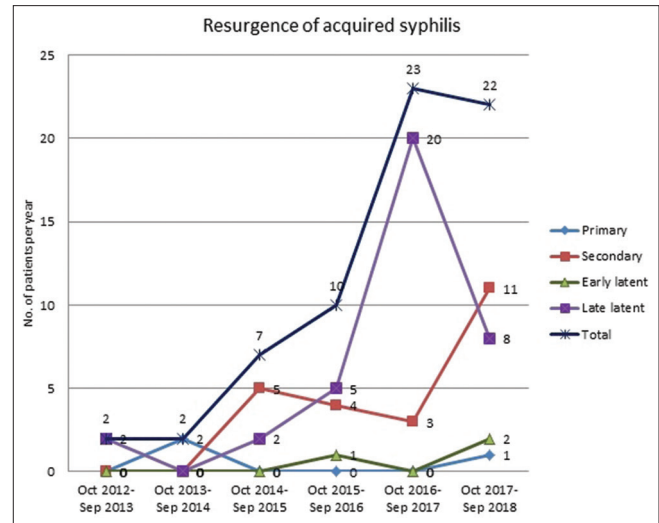


Figure 1: Number of acquired syphilis cases and their clinical staging reported from October 2012 to September 2018

Table 1: Proportion of syphilis in the first and second half of the study period

Stage of syphilis	Proportion of syphilis in the study period (n=total number of STIs)	
	First half (October 2012 - September 2015) (n=75), n (%)	Second half (October 2015 - September 2018) (n=140), n (%)
Primary	2 (2.7)	1 (0.7)
Secondary	5 (6.7)	18 (12.9)
Early latent	0	3 (2.1)
Late latent	4 (5.3)	33 (23.6)
Total	11 (14.7)	55 (39.3)

Table 2: Demographic details of patients with acquired syphilis during the study period (age group, marital status, and occupation)

Demographic details	Males (n=50)	Females (n=16)	Total (n=66), n (%)
Age group (years)			
<20	4	1	5 (7.6)
21-30	22	7	29 (43.9)
31-40	17	2	19 (28.8)
>40	7	6	13 (19.7)
Marital status			
Married	26	16	42 (63.6)
Unmarried	24	0	24 (36.4)
Occupation			
Manual laborers	23	1	24 (36.4)
Office clerk	11	2	13 (19.7)
Drivers	6	0	6 (0.9)
Traders	3	0	3 (0.4)
Students	2	0	2 (0.3)
Unemployed	5	0	5 (0.8)
Homemakers	0	13	13 (19.7)

of the 50 males and 5 (31.25%) of 16 females had more than one sexual partner. Twenty-eight males used condom occasionally during contact with their nonregular partners, while 22 never used condoms. Of the 66 patients with acquired syphilis, 3 (4.5%) had primary syphilis, 23 (34.8%) had secondary syphilis, and 40 (60.6%) had latent syphilis [Table 3].

There were no female sex workers (FSWs) in this study. None of the females in our study had same-sex behavior [Table 4]. Out of the 16 females, 5 (31.3%) were antenatal cases. Among the five antenatal cases, three (one case of secondary syphilis and two cases of latent syphilis) were detected before 36 weeks of pregnancy. The remaining two cases were detected after 36 weeks of pregnancy.

Out of 50 males, 29 (58%) were MSM. Of the 29 patients with MSM behavior, 17 (58.6%) had early syphilis, compared to 7 (33.3%) among 21 male patients without MSM behavior (Mantel–Haenszel Chi = 3.06; P = 0.04). There were no transgender or transsexual individuals in our study.

All three patients with primary syphilis were bisexual males who were active MSM and had only occasional heterosexual contacts. They presented with single painless chancres [Figure 2a].

Among the 23 patients of secondary syphilis, 18 (78%) were male. Out of these 18 males, 13 (72%) had same-sex behavior. Of the five female patients with secondary syphilis, one was pregnant. The skin lesions were predominantly papules in 20 (87%) patients. Figure 2b shows a patient with annular lesions on the beard area. Nine patients had psoriasiform lesions, and eleven had lichenoid papules on the palms and soles [Figure 2c]. The other clinical manifestations noted were mucosal erosions in five (22%) patients, of which three had oral erosions, one had erosion on the glans penis, and one had anal erosion. Ten (44%) patients had generalized lymphadenopathy.

Three cases of early latent and 37 cases of late latent syphilis were observed during the study period. RPR was reactive in all cases of early syphilis. Of the 37 patients with late latent syphilis, RPR was nonreactive in ten patients. The highest titer of 1:1024 was observed in a patient with secondary syphilis. A relatively high RPR titer of more than 1:16 was noted in eight cases of late latent syphilis. They included two patients diagnosed during routine antenatal checkup. Exact duration of syphilis could

not be ascertained in these two patients as their partners were seronegative. They were grouped under late latent syphilis. Two patients with latent syphilis who showed high RPR titer were HIV positive. The remaining four patients denied a history of sexual exposure and were grouped under syphilis of unknown duration and were treated as late latent syphilis. TPHA was positive in all patients.

Twenty (30.3%) out of 66 cases of acquired syphilis had coinfection with other STIs [Table 5]. HIV was the most common coinfection in our study (n = 15, 22.7%). Of the 15 cases who were HIV positive, one had primary, four had secondary, one had early latent, and nine had late latent syphilis.

Forty-eight (72.7%) patients were treated with doxycycline, 16 (24.2%) were treated with benzathine penicillin, and two patients were lost to follow-up before administering treatment. No instances of reinfection or relapse were noted in any patients during follow-up.

Discussion

According to this study spanning over 6 years from 2012, there is a steep increase in the number of cases of syphilis



Figure 2: (a) Primary chancre on the prepuce, (b) multiple annular plaques on the beard area, (c) syphilitic corneae on the palms

Table 3: Clinical staging of patients with syphilis

Stage of syphilis	Number of patients in each stage among males (n=50)	Number of patients in each stage among females (n=16)		Total number of patients in each stage (n=66), n (%)
		Nonpregnant (n=11)	Pregnant (n=5)	
Primary	3	0	0	3 (4.5)
Secondary	18	4	1	23 (34.9)
Early latent	3	0	0	3 (4.5)
Late latent	26	7	4	37 (56.1)

Table 4: Clinical stage of syphilis and its relationship with sexual behaviour

Stage of syphilis	Number of patients with heterosexual behavior (n=37), n (%)	Number of patients with same-sex behavior		
		Homosexual (n=10)	Bisexual (n=19)	Total (n=29), n (%)
Primary	0	0	3	3 (10)
Secondary	10 (27)	5	8	13 (45)
Early latent	2 (5.4)	1	0	1 (3)
Late latent	25 (67.6)	4	8	12 (42)

Table 5: Coinfection with other sexually transmitted infections and its relationship with sexual behavior

Coinfected STI	Number of heterosexual persons (n=37; 56.1%), n (%)	Number of persons with same-sex behavior			Total (n=66), n (%)
		Number among homosexuals (n=10)	Number among bisexuals (n=19)	Total (n=29; 43.9%), n (%)	
HIV	8 (21.6)	2	5	7 (24.1)	15 (22.7)
Condylomata acuminata	0	1	1	2 (6.9)	2 (3)
Herpes genitalis	1 (2.7)	1	0	1 (3.4)	2 (3)
Nongonococcal urethritis	0	0	1	1 (3.4)	1 (1.5)

STI=Sexually transmitted infection

from 2015 onward. Resurgence of syphilis was noticed in several studies from India and abroad.^[1-5,9] We also noticed an increase in the number of patients with early syphilis in the present study. Although late latent stage of syphilis outnumbered other stages of syphilis, a marked surge in the number of patients with early syphilis, especially of the secondary stage, was observed since 2015. Shah *et al.* had also reported early syphilis in 75 out of 110 (68.1%) patients with syphilis.^[4]

According to the CDC fact sheet 2017, 10.5% increase in the number of cases of early (primary and secondary) syphilis was reported between 2016 and 2017.^[10] The possible reasons for the recent increase in the prevalence of syphilis, mentioned in various studies, include an increased frequency of penooral and penoanal sex and an increased frequency of MSM and HIV coinfection.^[11] Kidd *et al.* have highlighted the high frequency of intravenous drug use among patients with primary and secondary syphilis.^[12] However, our study did not show such a finding.

In the present study, 76% of the cases were male. Male preponderance has been observed in several other studies from India and abroad.^[4,5,9] Of the 50 males, 29 (58%) were MSM (10 homosexuals and 19 bisexuals) and 21 were heterosexual. In the study by Muldoon and Mulcahy from Ireland between 2007 and 2009, 86.8% of cases of syphilis were among MSM. In a study by Shah *et al.* in 2013–2014, 22.7% were MSM.^[4] In a more recent study from South India, 104 (42.2%) out of 246 males were MSM with 32 having bisexual behavior.^[13] Increased prevalence of syphilis among MSM as observed in these studies and the present study underlines the need for strengthening targeted intervention (TI) programs in this population. The systematic review (2008) on MSM in India by Setia *et al.* suggested culturally sensitive prevention programs for controlling STIs among MSM as they had observed many MSM were forced to get married to females due to stigma and social issues associated with homosexuality.^[14] Recent decriminalization of homosexuality (2018) in India might have facilitated self-reporting of STIs, as well as destigmatization.^[15] It may also help in reducing the chance of getting married to monogamous females for social reasons and thereby reduce transmission of STIs among their female partners.

Several studies have reported a high frequency of coinfection of syphilis and HIV infection among MSM.^[5,10,16,17] This association results not only from the common modes of transmission but also from the increased frequency of unsafe sexual behavior among MSM infected with HIV.^[5,11] In a recent study by Saffren *et al.*, high prevalence (32.7%) of bacterial STIs and condomless sex was observed among MSM in urban India.^[18] In the present study, the most common STI found in association with syphilis was HIV (22.7%). Coexistence of HIV was found in 24.5% of cases by Shah *et al.* and 28.7% by Muldoon and Mulcahy.^[4,5] In our study, among the 15 cases of

coinfection of syphilis and HIV, 7 (46.7%) were MSM. Recently, there have been rapid developments of new point of care (POC) tests for STIs apart from the main ones for syphilis and HIV. Incorporation of these POC tests would help in early diagnosis and treatment of even asymptomatic STIs as coinfection with more than one STIs is common in the high-risk population.^[19]

Tracing and screening of partners are difficult among MSM. The increasing indulgence in oral sex is considered as an important factor contributing to the increase in syphilis.^[16] Oral sex is mistakenly considered as a “safe” sexual behavior by some persons. MSM are at higher risk of STIs because they indulge in diverse types of sexual behavior.^[20] Regular use of condom was low among both MSM and others in the present study. Condom use for oral sex should be an essential component of patient counseling to prevent STIs.^[16]

Interestingly, there were no FSWs in this study. A recent study from Tamil Nadu had 30% of FSWs among 85 females attending an STI clinic.^[13] The Government of Kerala conducts a TI program called Suraksha, under which FSWs are screened every 6 months for syphilis and HIV, and provided treatment if needed. Effectiveness of this program could be a possible reason why they do not attend the tertiary care hospital. Other possible reasons are practical difficulties and stigma among FSWs to attend STI clinics of tertiary care centers.

Although the number of females was low in our study, nearly one-third among them were antenatal cases. Other studies too have shown a high prevalence of syphilis in pregnancy.^[21,22] The most likely method of acquisition of disease among pregnant women is from their infected partners. The risk factors observed in other studies included the previous history of STIs, having multiple sex partners, sexual contact with MSM, and oral and intravenous drug use.^[21,22] Usually, women are screened for syphilis twice during pregnancy: in the first trimester and at term. The CDC and the American College of Obstetricians and Gynecologists recommend one more screening between 28 weeks and 32 weeks of gestation in communities and populations with a high prevalence of syphilis.^[7]

As there is a resurgence of syphilis in our population, early syphilis in antenatal cases may go undetected if VDRL or RPR are not done in dilution. As part of the routine antenatal checkup, nonspecific serological tests for syphilis are usually done in undiluted serum during the first trimester for all cases and third trimester in high-risk cases.^[8] Hence, it is advisable to do VDRL/RPR in dilution in antenatal cases with high risk.

Conclusion

We are witnessing an era of resurgence of syphilis. Physicians, researchers, and health administrators should work together to face this emerging challenge. Early

syphilis is especially more among MSM suggesting a need to strengthen targeted intervention programmes among them Antenatal screening should be more rigorous to prevent congenital syphilis.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

- Dhawan J, Khandpur S. Emerging trends in viral sexually transmitted infections in India. *Indian J Dermatol Venereol Leprol* 2009;75:561-5.
- Sharma VK, Khandpur S. Changing patterns of sexually transmitted infections in India. *Natl Med J India* 2004;17:310-9.
- Pialoux G, Vimont S, Moulignier A, Buteux M, Abraham B, Bonnard P. Effect of HIV infection on the course of syphilis. *AIDS Rev* 2008;10:85-92.
- Shah BJ, Karia DR, Pawara CL. Syphilis: Is it making resurgence? *Indian J Sex Transm Dis AIDS* 2015;36:178-81.
- Muldoon E, Mulcahy F. Syphilis resurgence in Dublin, Ireland. *Int J STD AIDS* 2011;22:493-7.
- Morhason-Bello IO, Kabakama S, Baisley K, Francis SC, Watson-Jones D. Reported oral and anal sex among adolescents and adults reporting heterosexual sex in sub-Saharan Africa: A systematic review. *Reprod Health* 2019;16:48.
- Workowski KA, Bolan GA, Centers for Disease Control and Prevention. Sexually transmitted diseases treatment guidelines, 2015. *MMWR Recomm Rep* 2015;64:1-137.
- WHO. The National Strategy & Operational Guidelines towards Elimination of Congenital Syphilis, Geneva: WHO; 2015. Monitoring and Evaluation Framework of E-PTCT of Syphilis. 25 February 2015; Available from: <https://www.aidsdatahub.org/sites/default/files/resource/india-elimination-congenital-syphilis-2015.pdf>. [Last accessed on 2020 Mar 30].
- Narayanan B. A retrospective study of the pattern of sexually transmitted diseases during a ten-year period. *Indian J Dermatol Venereol Leprol* 2005;71:333-7.
- Sexually Transmitted Diseases. Atlanta: CDC; 2017. Syphilis & MSM (Men Who Have Sex with Men) – CDC Fact Sheet 31 January 2017; Available from: <https://www.cdc.gov/std/syphilis/syphilismsm-2017.pdf>. [Last accessed 2020 Mar 30].
- Abara WE, Hess KL, Neblett Fanfair R, Bernstein KT, Paz-Bailey G. Syphilis trends among men who have sex with men in the United States and Western Europe: A Systematic review of trend studies published between 2004 and 2015. *PLoS One* 2016;11:e0159309.
- Kidd SE, Grey JA, Torrone EA, Weinstock HS. Increased methamphetamine, injection drug, and heroin use among women and heterosexual men with primary and secondary syphilis – United States, 2013-2017. *MMWR Morb Mortal Wkly Rep* 2019;68:144-8.
- Raju R, Rajaram M. Resurgence of syphilis in a tertiary care centre in South India – A retrospective study. *Int J Sci Stud* 2018;6:120-3.
- Setia MS, Brassard P, Jerajani HR, Bharat S, Gogate A, Kumta S, et al. Men who have sex with men in India: A systematic review of the literature. *J LGBT Health Res* 2008;4:51-70.
- Kealy-Bateman W. The possible role of the psychiatrist: The lesbian, gay, bisexual, and transgender population in India. *Indian J Psychiatry* 2018;60:489-93.
- Bjekić M, Šipetić-Grujičić S, Begović-Vuksanović B, Rafailović N, Vlajinac H. Syphilis resurgence in Belgrade, Serbia, in the new millennium: An outbreak in 2014. *Cent Eur J Public Health* 2017;25:277-81.
- Dougan S, Evans BG, Elford J. Sexually transmitted infections in Western Europe among HIV-positive men who have sex with men. *Sex Transm Dis* 2007;34:783-90.
- Safren SA, Devaleenal B, Biello KB, Rawat S, Thomas BE, Regenauer KS, et al. Geographic and behavioral differences associated with sexually transmitted infection prevalence among Indian men who have sex with men in Chennai and Mumbai. *Int J STD AIDS* 2021;32:144-51.
- Adamson PC, Loeffelholz MJ, Klausner JD. Point-of-care testing for sexually transmitted infections: A review of recent developments. *Arch Pathol Lab Med* 2020;144:1344-51.
- Wayal S, Reid D, Weatherburn P, Blomquist P, Fabiane S, Hughes G, et al. Association between knowledge, risk behaviours, and testing for sexually transmitted infections among men who have sex with men: Findings from a large online survey in the United Kingdom. *HIV Med* 2019;20:523-33.
- Trivedi S, Williams C, Torrone E, Kidd S. National trends and reported risk factors among pregnant women with syphilis in the United States, 2012-2016. *Obstet Gynecol* 2019;133:27-32.
- Benedetti KC, Ribeiro AD, Queiroz JH, Melo AB, Batista RB, Delgado FM, et al. High Prevalence of syphilis and inadequate prenatal care in Brazilian pregnant women: A cross-sectional study. *Am J Trop Med Hyg* 2019;101:761-6.