

Trends of syphilis seroprevalence at a tertiary care center in New Delhi, India: A 10-year analysis

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Abstract

Objectives: Syphilis has been called the great mimicker or the great imitator due to its myriad of clinical presentations. Despite strenuous concerted efforts toward the elimination of syphilis, it still remains a goal to be achieved. During recent years, many different trends of syphilis have been reported from around the globe. **Methods:** A retrospective observational clinico-investigative study was carried out to analyze the 10-year trends of syphilis at one of the largest public sector hospitals in India. **Results and Conclusion:** Both venereal disease research laboratory and *Treponema pallidum* Hemagglutination assay positivity rates showed a significant declining trend from 2007 to 2016, reflecting the success of the National Sexually Transmitted Infection Prevention and Control Program.

Key words: Epidemiology, seroprevalence, sexually transmitted infection, syphilis, trends of syphilis, *Treponema pallidum* hemagglutination

Introduction

In 2016, the World Health Organization released a new strategy to combat sexually transmitted infections (STIs) from 2016 to 2021. It prioritized the goal of 90% reduction in syphilis incidence globally and 50 or fewer cases of congenital syphilis/100,000 live births in 80% of countries by 2030.^[1] Syphilis remains an important public health challenge in low-income countries like India and has reemerged in several high-income countries during recent years. Syphilis, if left untreated, causes irreversible damage to the cardiovascular and central nervous systems, and perinatal deaths during pregnancy, and is associated with significant morbidity and mortality.^[2] The present study was undertaken to analyze the trends in prevalence, pattern and clinical presentations of syphilis, over 10 years, at a tertiary care hospital in India.

Methods

Study population

A retrospective observational clinico-investigative study was carried out at the Apex Regional STD Center, Safdarjung Hospital, New Delhi, India, wherein data from laboratory records of all the cases of STIs registered from January 2007 to December 2016 were analyzed.

Tests performed

All patients registered in STI clinic were routinely screened for syphilis using the venereal disease research laboratory (VDRL) test followed by the *Treponema pallidum* Hemagglutination assay (TPHA) as per the National STI Prevention and Control Program guidelines issued by the National AIDS Control Organization (NACO).

VDRL test (Institute of Serology, Kolkatta, and India) was performed as per the manufacturer's protocol. For VDRL testing, a blood sample was collected in a plain vacutainer, allowed to clot for 15 min, and centrifuged for 10 min at 2000 g. The VDRL antigen was prepared as per manufacturer recommendations. The flocculation test was performed on glass slides and the semiquantitative results were observed under a microscope.

The TPHA test was a standard Immutrep test (Omega Diagnostics Ltd., United Kingdom). Sera were diluted and mixed with *T. pallidum* sensitized formalized tanned fowl erythrocytes. Antibody to the sensitizing antigen, if present in the serum, caused agglutination of the cells. The cells formed a characteristic pattern in the bottom

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of the microtiter plate well and the results were read as positive. In the absence of antibody, they formed a compact button in the well and the results were read as negative.

Quality assurance

The Laboratory at Apex Regional STD Center is the Apex Reference Laboratory for STI Prevention and Control Program. The laboratory is also National Accreditation Board for Testing and Calibration Laboratories accredited for all its syphilis serological tests as per the ISO 15189:2013 standards.

As a part of external quality assurance, the laboratory has been participating successfully in the syphilis serology proficiency testing scheme conducted by the National Centre for Disease Control. As part of the internal quality check, known positive (low positive) and negative samples are run with each VDRL test batch. In the case of TPHA positive, negative kit controls are also run to validate the test results.

Statistical analysis

The STI counselor recorded complete epidemiological, clinical, and investigational data on predesigned validated pro forma. These data were analyzed statistically for changing epidemiological and clinical trends of syphilis. Trends of syphilis in different patient populations were obtained by calculating the percentage positivity during each year. Data entry was done using Microsoft Excel 2010 software, and statistical analysis was performed by applying the Chi-square test using SPSS version 20.0.

Results

From 2007 to 2016, over 10 years span, 373,845 patients were tested for syphilis, including 111,454 males and 262,391 females. The patients were divided into four age groups; ≤19 years were 5.5%. 20–29 years were 55.8%, 30–44 years were 31.6%, and ≥45 years were 7.1%.

Significantly greater number of males, 1.41% were VDRL reactive compared to 0.49% of females ($\chi^2 = 874.5, P < 0.0001$). VDRL reactivity showed a declining 10-year trend with 1.56% prevalence in 2007 and 1.05% in

2016 (χ^2 for trend = 87.8, $P < 0.0001$) with a significant fall in reactivity of both males and females [Figure 1a]. The VDRL positivity declined to 0.61% in 2014 and again started rising to 1.06% in 2016 [Figure 1b]. TPHA reactivity was 1.41% in 2007 which reduced to 1.09% by 2016, thus showing a declining trend (χ^2 for trend = 32.0, $P < 0.0001$) [Table 1 and Figure 1c].

Biological false positivity (BFP) was defined as VDRL reactive and TPHA nonreactive. The BFP rate was 0.07% overall. It was 0.06% in males and 0.10% in females. BFP was significantly more in females ($\chi^2 = 4.06, P = 0.043$) and in patients with VDRL titers <1:8 ($\chi^2 = 44.1, P < 0.0001$). TPHA positivity was higher with VDRL titers $\geq 1:8$ ($\chi^2 = 55.2, P < 0.0001$).

Based on clinical and laboratory testing, primary syphilis was diagnosed in 1.9% of cases, secondary in 5.3%, and latent in 92.8% of cases. Latent syphilis comprised 92.8% of total diagnosed cases ($P < 0.0001$) [Figure 1d] and 20–29 years was the most common age group for latent syphilis, with 55.8% cases ($P < 0.0001$).

Discussion

Syphilis infection is often asymptomatic, and therefore detection is often delayed and depends on the initiative of the individual and the capacity of the health system to promote and facilitate testing for early detection.

Globally, there is a decline of the bacterial STIs with an apparent increase of the viral STIs.^[3] The STI/reproductive tract infection (RTI) control strategy implemented in coordination with National Health Mission has helped achieve a significant decline in bacterial STIs. However, syphilis continues to remain a significant public health challenge in India.

The exact prevalence of syphilis in India is not known because of the stigma attached to the STIs, poor attendance at STI clinics, lack of a common registry for reporting STIs, and syndromic management which misses many asymptomatic cases.^[4] Hence, most of the studies from India involve only one group of patients and may not be representative of the true situation in the community.

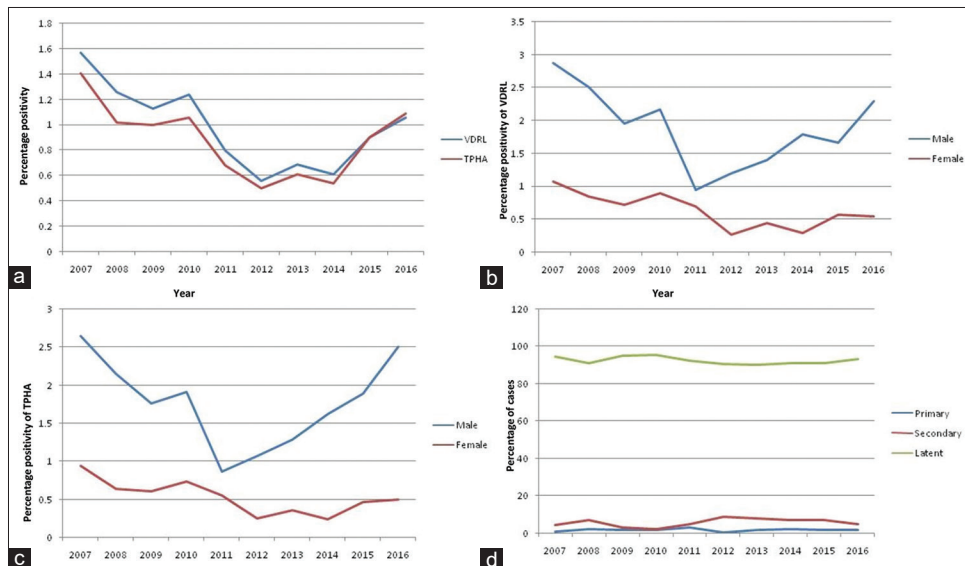


Figure 1: (a) Graph showing trend of VDRL and TPHA positivity (percentage) from 2007 to 2016, (b) Graph showing trend of VDRL positivity (percentage) in males and females, (c) Graph showing trend of TPHA positivity (percentage) in males and females, (d) Graph showing trend of primary, secondary, and latent syphilis (percentage). VDRL = Venereal disease research laboratory, TPHA = *Treponema pallidum* Hemagglutination assay

Table 1: Total number tested and venereal disease research laboratory and *Treponema pallidum* haemagglutination assay positivity from 2007 to 2016

Year	Total number tested		Number positive	
	Males	Females	Males (VDRL +/TPHA +), n (%)	Females (VDRL +/TPHA +), n (%)
2007	6441	17,050	185 (2.8)/171 (2.6)	183 (1)/161 (0.9)
2008	6054	18,472	152 (2.5)/130 (2.1)	156 (0.8)/119 (0.6)
2009	7859	15,589	153 (1.9)/139 (1.7)	113 (0.7)/95 (0.5)
2010	7657	20,084	166 (2.1)/147 (1.9)	178 (0.8)/147 (0.7)
2011	16,606	23,279	158 (0.9)/144 (0.8)	162 (0.7)/128 (0.5)
2012	10,148	22,957	122 (1.2)/109 (1)	63 (0.2)/57 (0.2)
2013	8047	22,514	113 (1.4)/104 (1.2)	99 (0.4)/82 (0.3)
2014	6090	22,274	109 (1.7)/99 (1.6)	65 (0.2)/54 (0.2)
2015	10,259	23,852	171 (1.6)/195 (1.9)	136 (0.5)/112 (0.4)
2016	11,017	26,234	252 (2.2)/276 (2.5)	141 (0.5)/130 (0.5)
Total	111,454	262,391	1581 (1.4)/1514 (1.3)	1296 (0.4)/1085 (0.4)

VDRL=Venereal disease research laboratory; TPHA=*Treponema pallidum* haemagglutination assay

The Spectrum-STI database for 2016 estimated 0.5% global prevalence of syphilis. A total estimated incident cases were 6.3 million (95% uncertainty interval: 5.5–7.1 million).^[5] Our study shows a comparable overall prevalence of 0.7% over 10 years.

There have been reports of increasing cases of syphilis in recent years, from different parts of the world, mainly the USA, Canada, China, Russia, parts of Europe, Australia, and Brazil.^[6] In the USA, the rate of primary and secondary syphilis decreased throughout the 1990s, reached an all-time low in 2000, and increased 11.1% in 2004–2005.^[7] In Brazil, there was a significant increase between 2010 and 2016, with 230,000 new cases of the disease being reported.^[8] Similar trends were reported from Europe, where the incidence of syphilis decreased dramatically during the 1980s, stabilized in the 1990s, and then increased since 1999–2000.^[9]

We found a few similar spikes in incidence during the 10 years period, although the overall trend was falling. The decline in syphilis numbers can be attributed to the excellent implementation and coverage of STI/RTI Prevention and Control Program. Furthermore, *T. pallidum* is susceptible to the antibiotics commonly used to treat other ailments in India. Over-prescription of these antibiotics could have helped in decreasing the prevalence and transmission of syphilis.

Many studies from India have found a decreasing trend of syphilis in the recent years. A study on 40,511 pregnant women from 1996 to 2005 in Chandigarh, North India, found that syphilis prevalence decreased significantly ($P < 0.01$) from 3% in 1996 to 0.84% in 2005.^[10] Another study from Rohtak, Haryana, reported that the annual distribution of syphilis showed a statistically significant decreasing trend from 2008 to 2012.^[11]

According to the NACO Annual Reports of India, the prevalence of syphilis among pregnant women attending antenatal care showed a spike in 2014–2015 and then fell again in 2016 (0.04% during 2013–2014, 0.23% in 2014–2015, and 0.15% in 2015–2016). The seroprevalence of syphilis is declining steadily among patients with STI/RTI, pregnant women, and high-risk groups. Designated STI/RTI clinics (DSRC), branded as “Suraksha Clinics,” reported 0.62% seroreactive rate in the 23 lakhs DSRC attendees screened during 2013–2014.^[12]

Some studies have stated no significant change in the prevalence. A study from Delhi reported the year-wise incidence of syphilis around 7%, exhibiting an almost uniform and stable trend over 5 years, from 2005 to 2009.^[13] Another study from Delhi reported no significant change in the trend of VDRL reactive cases over 9 years, from 2001 to 2009.^[14]

A rising trend of syphilis was reported from 2006 to 2011 at a tertiary care center in North India. Rising trend, although not statistically significant, was observed in pregnant women, drug users, and patients from wards/outpatient departments, while a statistically significant rise in the prevalence of syphilis was found in HIV-positive individuals. However, a falling trend (not statistically significant) was observed in STD clinic attendees.^[15]

Many studies from India have reported latent syphilis as the most common presentation of syphilis, accounting for up to 80%–90% of the cases.^[16,17] A recent study from Karnataka reported latent syphilis as the most common presentation (48.6%), and 20–29 years as the most frequently tested age group.^[18] We also found 92% cases of latent syphilis and 55.8% of patients in the 20–29 years of age group. A rampant inadvertent use of prescription and nonprescription antibiotics is prevalent in India. The resurgence of syphilis incognito or latent syphilis may be due to a partial cure of the disease by the widespread use of penicillins and cephalosporins for common infections.^[19]

The BFP rate shows gender association. The prevalence of BFP in females (0.1%) was significantly more than in males (0.06%) in our study. This is explained by elevated antinuclear antibodies, pregnancy, childbirth, puerperium, and diseases of the genitourinary system in females.^[20]

Conclusion

This study identifies a strong and significant downward trend in the seroprevalence of syphilis during 2007–2016. These results reflect that syphilis prevalence may be declining in the general population in the presence of the National STI Prevention and Control Program. Syphilis has features of a disease that could be eliminated, such as the absence of animal or environmental reservoir, 2–6 weeks’ incubation period, availability of inexpensive serodiagnostic tests, and treatable with a single dose of penicillin. The downward trend could be due to greater awareness, better education, and proper management of STIs. The decline could also be due to over-the-counter availability antibiotics, which has led to their more widespread use. Rapid diagnosis and treatment of infected individuals and their contacts are crucial to syphilis control programs.

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Conflicts of interest

There are no conflicts of interest.

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