

Epidemiology of great imitator (syphilis) in pregnancy in a tertiary care hospital, Tamil Nadu



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ABSTRACT

Background: Maternal syphilis remains a significant global public health concern due to its potential for vertical transmission, leading to serious adverse fetal outcomes. If left undiagnosed or untreated, it can result in stillbirth, low birth weight, premature birth, congenital syphilis, and neonatal mortality. Despite the availability of effective and affordable treatment with benzathine penicillin, missed opportunities for screening and treatment during pregnancy continue to contribute to preventable morbidity and mortality. **Aim and Objectives:** The objectives of this study were as follows: (1) To evaluate the epidemiological characteristics of antenatal women diagnosed with syphilis. (2) To analyze the influence of treatment timing on pregnancy outcomes. **Materials and Methods:** A descriptive study was conducted at a tertiary care hospital in Tamil Nadu from August 2018 to April 2024. Data were retrospectively collected from RTI/sexually transmitted infection (STI) clinic records. The sample size was 14,396 out of which antenatal cases were 2880 patients. All antenatal women who tested positive for both *Treponema pallidum* hemagglutination assay and rapid plasma reagin (RPR) were included. Details of maternal treatment and subsequent neonatal outcomes, including RPR titers and clinical features, were evaluated to assess the impact of early treatment. **Results:** Out of 14,396 new clients who attended the STI clinic during the study period, out of which 2880 (20%) are ANC cases. Three hundred and forty (2.3%) were found to be RPR reactive. Among these, 48 (14%) were antenatal women. Of these 48 pregnant women, 44 had live births, one had preterm live birth, two had preterm neonatal deaths, and one induced abortion due to congenital anomaly. The majority received timely treatment, and early intervention was associated with improved fetal outcomes. **Conclusion:** Early antenatal screening and prompt treatment of maternal syphilis are critical in preventing adverse fetal outcomes and eliminating congenital syphilis.

Key words: Maternal syphilis; Congenital syphilis; Benzathine penicillin; Antenatal screening

INTRODUCTION

Syphilis, known historically as the great imitator due to its wide range of clinical presentations, is a chronic infectious disease caused by the spirochete *Treponema pallidum*.

Despite the availability of a simple and effective cure – intramuscular benzathine penicillin – it continues to persist as a major global health challenge. The infection can remain asymptomatic for long periods, and when contracted during pregnancy, it carries a high risk of vertical transmission

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from mother to fetus, often with devastating consequences. Congenital syphilis results when *T. pallidum* crosses the placenta, leading to miscarriage, stillbirth, preterm labor, low birth weight, neonatal death, or long-term disabilities such as neurological impairment, skeletal deformities, or deafness.

Globally, syphilis has experienced a worrying resurgence, particularly in its early infectious stages. Recent surveillance data confirm a rising incidence in many parts of the world, with women of reproductive age being disproportionately affected.¹⁻³ In 2016, approximately 6.6 million infants were born with congenital syphilis – a number that reflects not only diagnostic and treatment gaps but also health system failures.⁴⁻⁶ By 2022, the World Health Organization (WHO) estimated 8 million cases of syphilis among adults aged 15–49 years and about 700,000 cases of congenital syphilis.^{7,8} In the same year, maternal syphilis contributed to over 390,000 adverse pregnancy outcomes, including stillbirths and neonatal deaths.

According to the WHO Global Health Observatory, an estimated 7.1 million adults were living with syphilis in 2020, with increasing prevalence noted among pregnant women.^{9,10} The growing burden of syphilis is not confined to low- and middle-income countries. In high-income settings, including the United States, similar trends have been observed. The U.S. Centers for Disease Control and Prevention (CDC) reported that in 2022 alone, more than 2.5 million cases of syphilis, gonorrhea, and chlamydia were recorded. Among these, the rate of syphilis in women giving birth had tripled since 2016, affecting nearly every age group, racial or ethnic category, and state.² In some countries, both maternal and congenital syphilis have reached epidemic proportions, further emphasizing the urgency for targeted public health interventions.

In response to this global health threat, the WHO launched a comprehensive strategy to eliminate congenital syphilis by 2030. The initiative includes three core targets: (1) Ensuring that 95% of pregnant women receive adequate antenatal care, (2) screening 95% of pregnant women for syphilis, and (3) treating at least 95% of those who test positive in a timely and appropriate manner.⁸ Despite these strategic goals and existing national guidelines such as those developed by the National AIDS Control Organization (NACO) in India, gaps remain in implementation, especially in rural or underserved populations. Early detection and timely intervention are crucial, as treatment initiated more than 4 weeks before delivery significantly reduces the risk of congenital syphilis and improves neonatal outcomes.

This study was therefore undertaken to contribute to the growing body of evidence on syphilis in pregnancy from

the Indian context, particularly in Tamil Nadu. It aims to evaluate the epidemiological characteristics of antenatal women diagnosed with syphilis attending a tertiary care hospital and to analyze the influence of treatment timing – whether early or late in pregnancy – on pregnancy outcomes.

Aims and objectives

The objectives of this study follows:

- 1) To evaluate the epidemiological characteristics of antenatal women diagnosed with syphilis.
- 2) To analyze the influence of treatment timing on pregnancy outcomes.

MATERIALS AND METHODS

This was a descriptive study conducted in the Department of Dermatology, Venereology, and Leprosy at K.A.P.V Government Medical College, Trichy from August 2018 to April 2024.

Data were retrospectively retrieved from patient-wise sexually transmitted infection (STI)/RTI clinic records, which included comprehensive documentation of patient details from the antenatal to postnatal period, including inpatient case files. The following data were collected: history of abortions, stillbirths, rapid plasma reagin (RPR) test details, and any previous treatment for syphilis.

Inclusion criteria were all antenatal women with serological evidence of syphilis, defined as reactivity on both:

- RPR test in quantitative titers, and
- *T. pallidum* hemagglutination assay (TPHA).

All included women received treatment with injection benzathine penicillin G, 2.4 million units, administered according to the stage of syphilis, in line with NACO guidelines. From February 2024 onward, as per revised national guidelines, all antenatal women diagnosed with syphilis were administered 3 weekly doses of benzathine penicillin regardless of clinical staging.

The women enrolled in the study were referred either from the antenatal clinic within the same hospital or from nearby government institutions and private healthcare facilities. All antenatal women included in the study underwent institutional delivery, and relevant details including neonatal RPR titers and clinical evaluation of the newborns were noted from hospital records.

In addition, one postnatal and one post-abortion woman who were seropositive and received treatment for syphilis were also included in the analysis.

Neonatal management was as follows:

- All syphilis-exposed infants received a prophylactic regimen of injection benzathine penicillin 50,000 units/kg body weight.
- Infants born to mothers treated <4 weeks before delivery were administered a curative regimen of injection crystalline penicillin, dosed at 50,000 units/kg body weight: Twice daily (BD) for the first 7 days, followed by 2 times daily (TDS) for the subsequent 3 days.

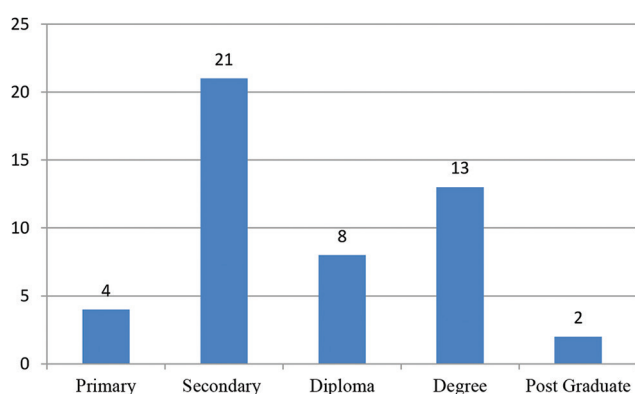
RESULTS

During the study period from August 2018 to April 2024, a total of 14,396 new clients attended the STI clinic, out of this 2880 cases were antenatal. Among them, 340 clients (2.3%) were reactive for the RPR test. Of this RPR-reactive group, 14% (n=48) were antenatal women. They were included in the study. The prevalence of RPR positive ANC cases was 1.6%.

Demographic and clinical characteristics

The age of participants ranged from under 20 to over 30 years. The highest proportion of cases (33.0%) was observed in the 26–30-year age group. The mean age of the study population was 26.04 years, with a standard deviation of 5.52 years (Table 1).

A majority of the women (43.8%) had attained secondary-level education. Notably, over 45% had completed higher secondary, diploma, or degree-level education, indicating a moderately educated antenatal population (Table 2).



The occupational distribution shows that the majority of women were homemakers (73.0%), while 27.0% were employed. This predominance of non-working status may influence healthcare utilization, health-seeking behavior, and access to timely antenatal screening and treatment services (Table 3).

Among the study participants, the majority were second gravida (47.9%), followed by primigravida (37.5%). Higher-

Table 1: Age distribution of antenatal women with syphilis

Age group	Number of women	Percentage
<20 years	11	23
21–25 years	12	25
26–30 years	16	33
>30 years	9	19
Total	48	100

Table 2: Educational status

Education level	Number of women	Percentage
Primary	4	8.2
Secondary	21	43.8
Diploma	8	16.7
Degree	13	27.1
Postgraduate	2	4.2

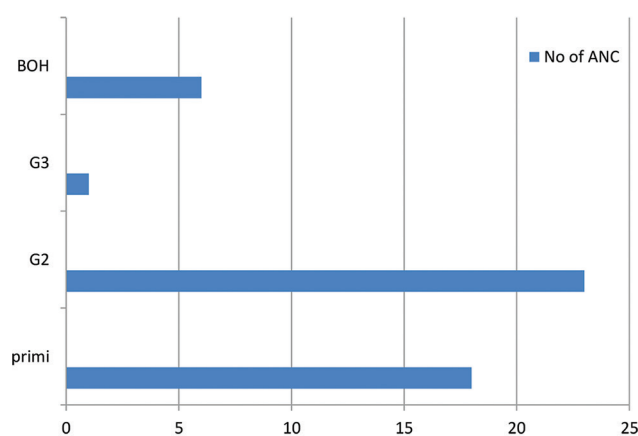
Table 3: Occupational status of antenatal women with syphilis

Occupation	Number of women (n)	Percentage
Homemaker	35	73.0
Working	13	27.0
Total	48	100.0

Table 4: Parity distribution of antenatal women with syphilis

Gravida	Number of women (n)	Percentage
Primigravida (G1)	18	37.5
Gravida 2 (G2)	23	47.9
Gravida 3 (G3)	1	2.1
Gravida ≥4 (G4+)	6	12.5
Total	48	100.0

order pregnancies (G3 and above) accounted for 14.6% of the cohort. The high proportion of multigravidas may be relevant in the context of previous undiagnosed syphilis in earlier pregnancies (Table 4).



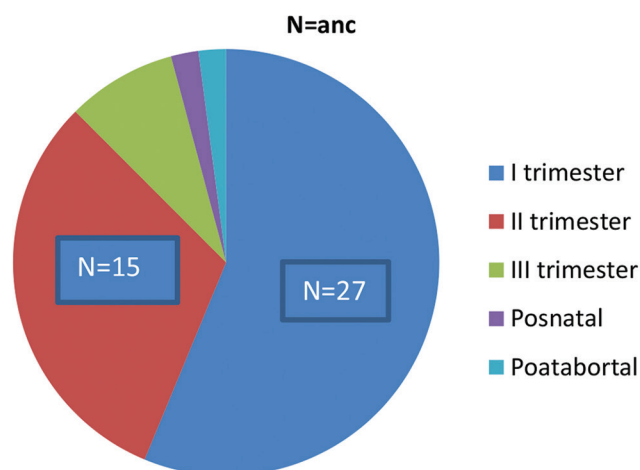
Of the 48 antenatal women included in the study, 31 women (64.6%) were diagnosed with early latent syphilis

and were treated with a single dose of benzathine penicillin except one patient who was treated with 3 weekly doses as per the revised guidelines. The remaining 17 women (35.4%) had late latent syphilis and received 3 weekly doses of benzathine penicillin, as per clinical staging and national guidelines.

A history of abortion was reported in 13 women (27.0%), and 7 women (14.5%) had a bad obstetric history (BOH), defined as more than two spontaneous abortions or a history of intrauterine fetal death (IUD). Notably, documentation regarding their previous Venereal disease research laboratory (VDRL) status and history of syphilis treatment was absent in all such cases. The observed association between BOH and syphilis in this cohort was statistically significant ($P<0.1$), highlighting the importance of early antenatal screening for syphilis to prevent recurrent adverse pregnancy outcomes (Table 5).

Among the study participants, high-risk sexual behavior was reported by two women, and 6.0% had clinically or serologically confirmed coexisting STIs. Specifically, one woman was diagnosed with human immunodeficiency virus (HIV), genital herpes, and genital molluscum contagiosum. Notably, none of the antenatal women presented with overt clinical signs of syphilis, reinforcing the critical need for routine serological screening in all pregnant women to ensure early detection and timely intervention (Table 6).

A majority of the antenatal women (56.25%) received syphilis treatment during the first trimester, and all of them had favorable fetal outcomes, delivering healthy infants. Among those who were treated in the second trimester (31.25%), there were two cases of neonatal death, both attributed to preterm birth and low birth weight. One woman received treatment in the postnatal period who had healthy infant. The post-abortion patient underwent medical



termination of pregnancy due to a diagnosed congenital anomaly – hypoplastic left heart syndrome (HLHS), identified on antenatal evaluation (Table 7).

All women had institutional delivery.

Among the 48 antenatal women in the study, 45 spouses were tested for syphilis. Of these, 25 men (55.6%) were reactive for both RPR and TPHA, and 15 men (33.3%) were reactive for TPHA alone. Five men (11.1%) were non-reactive. Three spouses were not willing for syphilis testing. Among the 40 serologically reactive partners, 28 (70%) were treated with benzathine penicillin, while the remaining men were managed with oral doxycycline 100 mg twice daily, due to injection refusal.

Treatment compliance among antenatal women was 100%, which was statistically significant ($P=0.001$). Women diagnosed with the early latent syphilis received a single intramuscular dose of benzathine penicillin 2.4 million units and were treated with a single dose of benzathine penicillin except one patient who was treated with 3 weekly doses as per the revised guidelines, whereas those with late latent syphilis were administered 3 weekly doses, following NACO guidelines (Table 8).

Table 5: Type of syphilis among antenatal women

Type of syphilis	Number of women (n)	Percentage
Early latent syphilis	31	64.6
Late latent syphilis	17	35.4
Total	48	100.0

Table 6: Associated STIs

Associated genital lesion	Number of antenatal women
HIV	1
Genital herpes	1
Genital molluscum	1
Other STIs	2

STIs: Sexually transmitted infections, HIV: Human immunodeficiency virus

Table 7: Gestational age at treatment and corresponding fetal outcomes

Gestational age at treatment	Number of women treated (%)	Fetal outcome
First trimester	27 (56.25)	27 live births
Second trimester	15 (31.25)	12 live births, 1 preterm live birth, and 2 preterm neonatal deaths
Third trimester	4 (8.3)	4 live births
Postnatal	1 (2.0)	1 live birth
Post-abortion	1 (2.0)	1 congenital anomaly (HLHS)

HLHS: Hypoplastic left heart syndrome

Table 8: Serological status and treatment of spouses

Spousal serological status	Number of men (n)
Both RPR and TPHA reactive	25
TPHA-reactive only	15
Non-reactive on both tests	5
Not tested	3
Total spouses tested	45
Spouses treated with penicillin	28

RPR: Rapid plasma reagin, TPHA: *Treponema pallidum* hemagglutination assay

Outcome of this pregnancy

The mean gestational age at delivery was 39 weeks and the average birth weight of babies was 3 kg.

Among the 48 antenatal women treated for syphilis, adverse fetal outcomes were observed in 4 cases (8.3%). Three neonates were born preterm with low birth weight, all of whom had been delivered by mothers who received treatment during the second trimester. Of these three, two neonates died due to hypoxic-ischemic encephalopathy, while one survived.

One woman, treated during the first trimester, underwent a medically indicated abortion due to the detection of a severe congenital cardiac anomaly—HLHS. None of the baby had clinical signs of congenital Syphilis at birth and also on follow-up (Table 9).

DISCUSSION

In the present study, involving antenatal women diagnosed with syphilis, the most common age group was 26–30 years (33%), similar to the findings of Hasan Berkan in Turkey, reflecting the global trend of syphilis affecting women in the reproductive age group. Among the study participants, 24 had education beyond secondary school, which aligns with reports suggesting increasing STI incidence even in educated populations.¹⁻³

The majority of the women were referred from Primary Health Centers or from the obstetrics department, with most being diagnosed in the first trimester, indicating committed antenatal care services. Early antenatal registration and routine screening for syphilis, HIV, and hepatitis B surface antigen contributed to favorable fetal outcomes in this study.

The overall RPR reactivity among pregnant women screened in our setting was 0.19%, which aligns with the NACO HIV Sentinel Surveillance Plus 2021 data reporting a syphilis prevalence of 0.1% (95% confidence interval: 0.09–0.11) among antenatal women in India.² This is also consistent with a study conducted by Palakkal et al.³

Table 9: Adverse fetal outcomes and timing of maternal syphilis treatment

Adverse fetal outcome	Number of babies	Gestational age at maternal treatment
Preterm, low birth weight	3 (including two neonatal deaths)	Second trimester
Congenital anomaly (HLHS)*	1	First trimester

*HLHS: Hypoplastic left heart syndrome

Of the women treated, 95.6% delivered healthy neonates. All women who received treatment during the first trimester delivered live-born infants, except for one who underwent an induced abortion due to HLHS – a congenital cardiac anomaly with a well-established genetic origin, making syphilis an unlikely cause.^{5,6} This case underscores the importance of comprehensive antenatal anomaly screening in women diagnosed with infections during pregnancy.

Early prenatal care and timely treatment significantly improve fetal outcomes in maternal syphilis. Missed or delayed screening and treatment represent lost opportunities to prevent congenital syphilis, as emphasized in CDC and WHO guidelines.^{4,10,11} In our study, 7 women (14.5%) had a BOH – defined as two or more spontaneous abortions or intrauterine deaths – and all had live births in the current pregnancy after receiving three doses of benzathine penicillin, supporting the effect of treatment.^{11,12} However, due to a lack of previous VDRL/treatment documentation, whether these cases follow Kassowitz law could not be ascertained.

Among those treated in the second trimester, 20% (3 women) had adverse fetal outcomes, such as preterm birth and low birth weight, though all were second gravidae with prior live births. These women were diagnosed with early latent syphilis, consistent with literature showing that early treatment reduces the risk of preterm birth by 52% and stillbirth by 79%, as evidenced by a 2023 meta-analysis.⁷

Interestingly, the four women treated during the third trimester, all with late latent syphilis, gave birth to live neonates. This correlates with the non-infectious nature of late latent syphilis and the reduced risk of transmission at that stage.^{12,13}

Partner screening and treatment is a critical component of congenital syphilis prevention, yet often remains suboptimal. In our cohort, only 72% (n=28) of seropositive male partners were treated with benzathine penicillin, while others received doxycycline or no treatment due to refusal. This underscores the challenges of partner management, despite WHO and CDC emphasizing its importance in STI control strategies.^{8,10,13}

CONCLUSION

Congenital syphilis is entirely preventable through early diagnosis, appropriate treatment, and follow-up of both pregnant women and their partners. This requires a coordinated, multidisciplinary effort involving maternal and child health services, STI and HIV prevention programs, and reproductive healthcare providers. The findings of this study strongly support that early screening during pregnancy, especially in the first trimester, followed by prompt treatment with injection benzathine penicillin, significantly reduces the risk of adverse fetal outcomes. Strengthening antenatal care systems and ensuring partner management remain pivotal to the elimination of congenital syphilis.

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Authors' Contributions:

UBZ- Definition of intellectual content, literature survey, prepared first draft of manuscript, implementation of study protocol, data collection, data analysis, manuscript preparation, and submission of article; **MNY**- Concept, design, clinical protocol, manuscript preparation, editing, and manuscript revision; **SDH**- Design of study, statistical analysis, and interpretation; **HR**- Review manuscript; **RB**- Review manuscript; **NN**- Literature survey and preparation of figures; and **AS**- Coordination and manuscript revision.

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