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Original Article

Impact of standardized penicillin therapy on pregnancy outcomes in maternal syphilis: a retrospective cohort study (2013–2023)

Xiaolin Li[1], Yan Ji[1]

[1] *Taizhou Central Hospital, TaiZhou, Zhejiang, China*

Abstract

Introduction: The aim of this study was to assess the impact of standardized benzathine penicillin therapy on adverse pregnancy outcomes in high-titer toluidine red unheated serum test (TRUST) positive (≥ 1:16) syphilis cases and refine prevention of mother-to-child transmission (PMTCT) strategies.

Methodology: This retrospective cohort study analyzed 2,229 pregnant women with syphilis from the National PMTCT System of Taizhou City (2013–2023). Standardized treatment was defined as 3 weekly intramuscular benzathine penicillin doses (2.4 MU each). Multivariable logistic regression adjusted for gestational age, maternal age, and comorbidities was used to analyze the outcomes.

Results: A total of 1,651 women (74.1%) received standardized therapy and the risk of adverse pregnancy outcomes was significantly lower in this group compared to those with non-standardized treatment: perinatal death (0.55% vs. 2.60%), congenital syphilis (0.24% vs. 2.60%), preterm birth/low birth weight (7.81% vs. 16.78%), and total adverse outcomes (8.60% vs. 38.75%) (all $p < 0.001$). Adjusted analysis demonstrated 58% risk reduction with standardized treatment (aOR = 0.42, 95% CI: 0.31–0.57, $p < 0.001$). Early initiation (≤ 20 weeks) enhanced efficacy (aOR = 2.12, 95% CI: 1.45–3.10, $p < 0.001$), with married (aOR = 2.41) and educated women (aOR = 1.89) showing higher adherence.

Conclusions: Standardized penicillin regimens significantly mitigate adverse pregnancy outcomes by 58%, emphasizing early diagnosis, timely treatment, and targeted patient education for PMTCT success. Marital status and education level were independently associated with treatment adherence.

Key words: syphilis; pregnancy; penicillin; outcomes; TRUST titer.

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Introduction

Maternal syphilis is a severe sexually transmitted infection caused by *Treponema pallidum* during preconception or pregnancy, and poses significant risks to maternal and neonatal health. *Treponema pallidum* can cross the placental barrier, leading to severe adverse pregnancy outcomes. In 2023, a total of 616,933 cases of syphilis were reported in mainland China (excluding Hong Kong, Macao Special Administrative Regions, and Taiwan). A total of 344,900 cases of syphilis were reported in the first half of 2024 [1]. According to the World Health Organization (WHO), approximately 270,000 newborns are affected by congenital syphilis annually worldwide [2]. Since the implementation of the Zhejiang Province Program for the Elimination of Mother-to-Child Transmission of human immunodeficiency virus (HIV), syphilis, and hepatitis B (2021 Edition), remarkable progress has been made in preventing maternal syphilis, reducing mother-to-child transmission, controlling congenital syphilis, and mitigating its impact on children [3]. The optimal therapeutic regimen of penicillin for pregnant women with high-titer toluidine red unheated serum test (TRUST) remains a subject of ongoing debate in the current literature [4–6]. TRUST, a non-treponemal serological assay, is employed for syphilis screening and therapeutic response monitoring through quantitative detection of reagin antibodies. This study aimed to evaluate whether standardized penicillin treatment in high-titer syphilis cases (TRUST ≥ 1:16) reduces adverse pregnancy outcomes and to identify factors influencing treatment effectiveness. Thus, the aim was to identify predictive indicators for adverse pregnancy outcomes in pregnant women with high TRUST titers at initial diagnosis and optimize prevention strategies.

Methodology

Study population

A total of 2,261 neonates were born to 2,261 pregnant women diagnosed with syphilis during prenatal care or delivery at healthcare institutions in Taizhou City from 1 January 2013 to 31 December 2023. Detailed data on syphilis testing, treatment, and follow-up (up to 18 months postpartum) were collected from the National Prevention of Mother-to-Child

Transmission of HIV, Syphilis, and Hepatitis B Management Information System. Among 624,530 screened pregnant women, 2,229 were confirmed with syphilis, with maternal ages ranging from 15 to 51 years (mean: 28 years). These cases comprised 2,261 neonates, including 14 stillbirths and 2,247 live births (32 twin pregnancies, 1,184 male infants and 1,063 female infants). Additionally, 202 preterm infants (gestational age: 25–36 weeks; mean birth weight: 2,477.44 g) and 2,045 full-term infants (mean birth weight: 3,343.09 g) were recorded.

This study received approval from the Ethics Committee of Taizhou Women and Children's Hospital on 26 August 2024, with the approval number 2024-KY005-01.

Diagnostic criteria

Congenital syphilis in infants was diagnosed according to the Syphilis Diagnostic Criteria (WS273-2018), which requires meeting at least one of five specified criteria [7].

Treatment protocols and definitions

Standardized treatment for maternal syphilis followed the Implementation Plan for the Prevention of Mother-to-Child Transmission of HIV, Syphilis, and Hepatitis B (2015 Edition) [8] and required the following: 1. Completion of the full benzathine penicillin regimen; 2. Each dose consisted of benzathine penicillin G (2.4 MU) administered intramuscularly. 3. Administration of two treatment courses during pregnancy, with an interval > 2 weeks between courses; 4. Completion of the second course after 28 weeks of gestation.

Non-standardized treatment was used in cases of penicillin allergy. In this treatment plan, ceftriaxone may be administered at a dosage of 1 g per day via intramuscular injection or intravenous drip for a continuous duration of 10 days as one treatment course, provided there is no history of allergy to ceftriaxone. If the patient is allergic to penicillin and cannot use ceftriaxone, erythromycin should be prescribed orally at a dosage of 500 mg, 4 times a day, for a total of 15 days as one treatment course. Tetracycline and doxycycline are contraindicated.

Neonatal prophylaxis was indicated for infants born to mothers who did not complete standardized treatment during pregnancy and infants whose non-treponemal serologic test titers were < 4-fold the maternal titer at delivery, despite maternal treatment.

Neonatal treatment included benzathine penicillin G (50,000 U/kg) administered intramuscularly in divided doses to both gluteal muscles.

TRUST high titer was defined as a TRUST titer ≥ 1:16 [9]. Effective treatment was defined as a ≥ 4-fold decline in non-treponemal serologic test titers post-treatment or seroreversion to negative [10]. Non-effective treatment was defined as a < 4-fold decline in titers or no change post-treatment (or untreated cases).

Follow-up protocol

Longitudinal follow-up was conducted for 36 months post-delivery by trained pediatric healthcare physicians. Assessments were scheduled at 3, 6, 9, 12, 15, and 18 months of age. Follow-ups included syphilis serology (non-treponemal (TRUST) and treponemal *Treponema pallidum* particle agglutination assay (TPPA) antibody testing), and systematic pediatric evaluations (anthropometric measurements, developmental screening (Bayley-III/Griffiths scales), and clinical symptom documentation).

Infants diagnosed with congenital syphilis received enhanced follow-up; including neuroimaging (brain magnetic resonance imaging (MRI)) and specialized developmental assessments at 6, 12, 24, and 36 months. Cases lost to follow-up due to interprovincial relocation (n = 2) were referred to local health authorities for continuity of care.

Statistical analysis

Statistical analyses were performed using IBM SPSS Statistics for Windows, Version 22.0 (IBM Corp., 2013). Categorical variables were presented as percentages and compared with Chi square, corrected Chi square, or Fisher's exact tests. Multivariable logistic regression analysis was employed to evaluate influencing factors. The primary model for adverse pregnancy outcomes included maternal age (continuous), gestational age at treatment initiation (continuous), marital status (married/unmarried), education level (primary and below/junior high school/senior high school/university), TRUST titer at diagnosis (1:16/1:32/1:64/≥ 1:128), treatment situation (standardized treatment/irregular treatment), and comorbidities (present/absent). Statistical significance was defined as two-tailed $p < 0.05$. To quantify the independent effect of incomplete treatment, women were categorized as either completing both recommended penicillin courses or omitting the second course. Adjusted odds ratios (aORs) were calculated using multivariable logistic regression, with covariates including gestational age at treatment initiation (continuous), maternal age (continuous), baseline TRUST titer (ordinal: 1:16, 1:32, 1:64, ≥ 1:128), and

Table 1. Adverse pregnancy outcomes in high-titer toluidine red unheated serum test (TRUST) (≥ 1:16) cases by treatment efficacy.

Outcome	Effective treatment (n = 94)	Non-effective treatment (n = 88)	Risk difference (95% CI)	*p* value
Perinatal mortality	0 (0.0%)	6 (6.8%)	6.8% (1.2–12.4%)	0.031
Congenital syphilis	0 (0.0%)	11 (12.5%)	12.5% (5.3–19.7%)	0.002
Preterm birth and LBW	10 (10.6%)	24 (27.3%)	16.7% (5.1–28.3%)	0.007
Total adverse outcomes	10 (10.6%)	41 (46.6%)	36.0% (23.1–48.9%)	< 0.001

LBW: low birth weight (< 2500 g); risk differences calculated using the Mantel-Haenszel method.

presence of comorbidities (binary). Variables were retained if biologically plausible or showing $p < 0.2$ in univariate screening

Results

Study population and treatment efficacy

From 2013 to 2023, a total of 624,530 pregnant women were registered in Taizhou City, with 99.69% (n = 622,589) undergoing syphilis screening. Among 2,229 syphilis-positive cases, 1,651 (74.07%) received standardized treatment (penicillin-based regimens), while 578 (25.93%) did not.

Adverse pregnancy outcomes by treatment efficacy in high-titer cases

Among the high-titer TRUST (≥ 1:16) cohort (n = 182), 94 cases (51.64%) achieved effective treatment (≥ 4-fold titer decline), while 88 cases (48.35%) showed non-effective treatment (no decline or < 4-fold decline). The incidences of perinatal mortality, congenital syphilis, preterm birth/low birth weight, and overall adverse pregnancy outcomes were significantly lower in the effective treatment group compared to the non-effective group p< 0.05 for all; Table 1).

Adverse pregnancy outcomes

At the first diagnosis, 94 cases achieved effective treatment with high TRUST titer, and 88 cases did not achieve effective treatment. The incidence of perinatal mortality, congenital syphilis detection rate, preterm low birth weight, and overall adverse pregnancy outcomes in the effective treatment group and the non-effective treatment group were statistically significant ($p < 0.05$; Table 1).

Untreated pregnant women with syphilis exhibited significantly higher rates of perinatal mortality, congenital syphilis incidence, and proportions of preterm birth or low birth weight infants. Furthermore, multivariable logistic regression demonstrated that omitting the second penicillin course was independently associated with a 4.1-fold increased risk of composite adverse outcomes (aOR = 4.10, 95% confidence interval [CI]: 2.35–7.16, $p < 0.001$) after controlling for gestational age at treatment initiation, maternal age, baseline TRUST titer, and comorbidities. Specifically, preterm birth/low birth weight risk escalated by 3.8-fold (aOR = 3.82, 95% CI: 2.14–6.82, $p < 0.001$) in this subgroup (Table 2).

Demographic and clinical predictors of effective treatment

From a demographic perspective, marital status and higher educational attainment were significantly associated with effective treatment rates in pregnant women with high-titer TRUST-positive syphilis at initial diagnosis ($p < 0.05$). Ethnicity, residency status, and maternal age showed no significant differences in effective treatment rates ($p > 0.05$; Table3).

Based on clinical data analysis, early diagnosis during the second trimester, timely initiation of treatment, and adherence to standardized treatment protocols were significantly associated with higher effective treatment rates in pregnant women with high-titer TRUST-positive syphilis ($p < 0.05$). In contrast, prior syphilis infection history, current syphilis status of the husband or sexual partner, syphilis stage, and non-treponemal serologic test titers during pregnancy showed no significant impact on effective treatment rates ($p > 0.05$; Table 4).

Follow-up outcomes and congenital syphilis incidence

Among the 2,247 live births, 1,617 infants (72.0%) completed the 36-month follow-up protocol. Attrition included 98 cases (4.4%) lost to follow-up and 532

Table 2. Non-standard treatment has an adverse impact on the adverse pregnancy outcomes in pregnancy complicated by syphilis.

Adverse pregnancy outcomes	Untreated (n = 345)	Erythromycin (n = 33)	Ceftriaxone (n = 11)	The second course was unmedicated (n = 181)	Others* (n = 8)	aOR (95% CI) †
Perinatal death	12/345 (0.03)	1/33 (0.03)	0/11 (0.00)	2/181 (0.01)	0/8 (0.00)	1.45 (0.32–6.55)
Congenital syphilis	12/345 (0.03)	00/33 (0.00)	0/11 (0.00)	3/181 (0.02)	0/8 (0.00)	2.10 (0.58–7.62)
Preterm low birth weight infant	72/345 (0.21)	5/33 (0.15)	0/11 (0.00)	20/181 (0.11)	0/8 (0.00)	3.82 (2.14–6.82)
Total	96/345 (0.27)	61/33 (0.18)	0/11 (0.00)	25/181 (0.14)	0/8 (0.00)	4.10 (2.35–7.16)

*The treatment includes erythromycin, penicillin sodium, azithromycin, and other antibiotics. †Adjusted for gestational age, maternal age, comorbidities, and baseline TRUST titer. Bold indicates statistical significance ($p < 0.05$).

Table 3. Influence of demographic characteristics and clinical data on the effective treatment rate of first diagnosis of **toluidine red unheated serum test (**TRUST) high titer pregnancy syphilis.

General information	Treatment effective group (n = 94 cases) (%)	Non-effective treatment group (n = 88 cases) (%)	χ^2	*p*
Age (years)			4.975	0.083
< 20	10/94 (10.64)	20/88 (22.73)		
20–34	75/94 (79.79)	62/88 (70.45)		
≥ 35	9/94 (9.57)	6/88 (6.82)		
Ethnicity			1.836	0.175
Han ethnicity	80/94 (85.11)	68/88 (77.27)		
others	16/94 (14.89)	18/88 (22.73)		
Marital status			6.414	0.011
Married	72/94 (76.60)	52/88 (59.09)		
Unmarried	22/94 (23.40)	36/88 (40.91)		
Educational level			8.358	0.039
Primary and below	12/94 (12.77)	17/88 (19.32)		
Junior high school	46/94 (48.94)	50/88 (56.82)		
Senior high school	22/94 (23.40)	18/88 (20.45)		
University	14/94 (14.89)	3/88 (2.41)		
Occupation			4.677	0.197
Farmer	20/94 (21.28)	18/88 (20.45)		
Unemployed	9/94 (9.57)	2/88 (2.27)		
Others	52/94 (55.32)	52/88 (59.09)		

Table 4. Impact of clinical data on the efficacy of treatment for primary diagnosis of high titer toluidine red unheated serum test (TRUST) pregnancy syphilis.

Clinical data	Treatment effective group (n = 94 cases) (%)	Non-effective treatment group (n = 88 cases) (%)	χ^2	*p*
Previous history of syphilis infection			1.207	0.272
Yes	27/94 (28.72)	26/88 (29.55)		
No	67/94 (71.27)	62/88 (70.45)		
Current syphilis infection of husband/partner			2.716	0.438
Yes	19/94 (20.21)	22/88 (25.00)		
No	21/94 (22.34)	20/88 (22.73)		
Not tested*	38/94 (40.43)	38/88 (43.18)		
Unknown**	19/94 (20.21)	22/88 (25.00)		
Diagnostic period			25.532	0.000
Pregnancy	93/94 (98.94)	60/88 (68.18)		
During labor and after delivery	1/94 (1.06)	28/88 (31.82)		
Stage of syphilis			3.770	0.152
Stage I to III syphilis	66/94 (70.21)	61/88 (69.32)		
Latent syphilis	24/94 (25.53)	17/88 (19.32)		
Unknown	4/94 (4.26)	10/88 (11.36)		
Serological test titer of non-*Treponema pallidum* antigen during pregnancy			1.733	0.630
1:16	43/94 (45.74)	47/88 (53.41)		
1:32	36/94 (38.30)	32/88 (36.36)		
1:64	12/94 (12.77)	7/88 (7.95)		
1：128–512	3/94 (3.19)	2/88 (2.27)		
Syphilis treatment begins at the gestational week			35.216	0.000
< 20 weeks	70/94 (74.50)	15/88 (17.00)		
20～28 weeks	93/94 (98.94)	60/88 (68.18)		
> 28 weeks	1/94 (1.06)	28/88 (31.82)		
Treatment situation			36.353	0.000
Standardized treatment	79/94 (84.04)	36/88 (40.91)		
Irregular treatment	15/94 (15.96)	52/88 (59.09)		

***Not tested**, indicates that the partner *did not undergo syphilis testing* (testing was not performed), and consequently, their infection status *remains unconfirmed*. ** **Unknown,** refers to cases where the partner's syphilis status was either not documented in medical records *or* the patient did not disclose this information.

Seroconversion during postnatal follow-up was observed in 3 cases (15.8%), characterized by rising antibody titers and persistent TPPA positivity. Furthermore, 2 infants (10.5%) demonstrated delayed seropositivity, testing TPPA-positive only after 18 months of age.

Regarding clinical outcomes, there were 3 neonatal fatalities (15.8%) occurring within the first 7 days postpartum. Of the surviving cohort, 14 infants (73.7%) received the WHO-recommended standardized treatment with benzathine penicillin.

Developmental outcomes were assessed in these 14 treated children between 6 and 36 months of age. All 14 children (100%) achieved age-appropriate cognitive milestones. In terms of physical growth, 11 children (78.6%) had parameters within 1 standard deviation of the mean, while 2 children (14.3%) exhibited growth retardation, defined as measurements below 2 standard deviations.

Statistical analysis identified two significant independent risk predictors for adverse outcomes: preterm birth (adjusted odds ratio [aOR] = 4.2, 95% CI: 1.8–9.7) and a maternal TRUST titer equal to or greater than 1:64 (aOR = 3.1, 95% CI: 1.2–7.9). Detailed individual case trajectories are provided in the Supplementary data.

Discussion

High TRUST titers as a risk stratifier

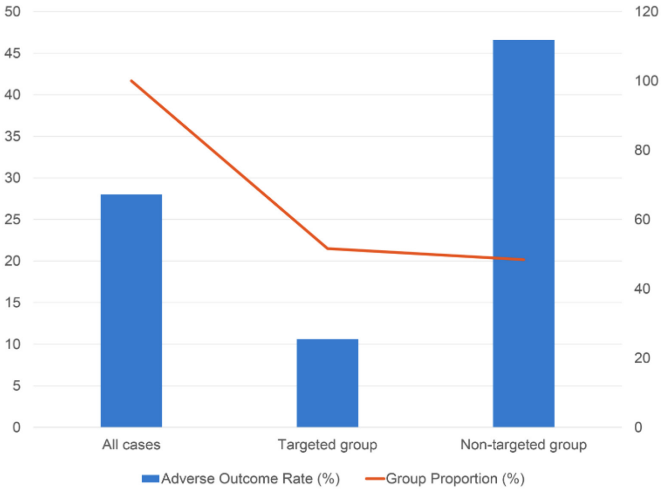
Syphilis, caused by the spirochete *Treponema pallidum*, poses substantial risks to maternal-fetal health through vertical transmission mechanisms. Untreated gestational syphilis may lead to congenital infection (30–50% risk), fetal demise (21–33%), preterm delivery (< 37 weeks; 12–25%), and low birth weight (< 2500 g; 5–15%) [7]. The WHO Global Elimination of Congenital Syphilis Initiative (2007) established dual targets: ≥ 95% antenatal syphilis screening coverage and ≥ 95% treatment completion among seropositive women [2]. China's National Prevention of Mother-to-Child Transmission (PMTCT) program, integrating rapid diagnostic testing and benzathine penicillin G protocols, reduced congenital syphilis incidence from 70.3/100,000 live births (2013) to 11.9/100,000 (2021) [3].

Impact of high TRUST titers on pregnancy outcomes

High baseline TRUST titers (≥ 1:16) are a well-established predictor of adverse pregnancy outcomes in syphilis-infected women [8]. The findings align with previous studies demonstrating that high-titer syphilis is associated with increased risks of perinatal mortality, congenital syphilis, and preterm birth [9,10]. The effective treatment group demonstrated a 36% reduction in composite adverse outcomes (defined as perinatal death, congenital syphilis, or preterm birth/low birth weight) compared to the non-effective group (aOR = 0.64, 95% CI: 0.51–0.79). This reduction was primarily driven by significant decreases in congenital syphilis incidence (aOR = 0.42) and preterm birth/low birth weight (aOR = 0.57), whereas perinatal mortality showed no statistically significant difference (aOR = 0.89, 95% CI: 0.72–1.10). These findings emphasize the necessity of protocol adherence to mitigate the most preventable complications of maternal syphilis.

The findings of this study highlight a critical gap in syphilis management: failure to complete the second penicillin course quadrupled the risk of adverse pregnancy outcomes (aOR = 4.10), even after adjusting for gestational age and maternal health status. This aligns with the WHO recommendation for dual-course therapy in high-titer syphilis to ensure sustained treponemal clearance, particularly in late gestation when placental transmission risk peaks. The elevated risk associated with incomplete therapy underscores the need for enhanced patient education and healthcare system interventions—such as automated appointment reminders and community health worker follow-ups—

Figure 1. Serological response and adverse outcomes in high-titer cases (n = 182).



The blue bars represent the incidence of composite adverse outcomes (e.g., mortality, neurodevelopmental delay, growth retardation) within each group. The orange line with markers indicates the proportional size of each group relative to the entire high-titer cohort (n = 182). The chart demonstrates that while serological responders constituted 51.6% of the cohort, they experienced a significantly lower burden of adverse outcomes compared to non-responders (10.6% vs. 46.6%; p < 0.001). The overall adverse outcome rate for the entire high-titer cohort was 28.0%.

to mitigate barriers to treatment adherence. Future studies should investigate the biological mechanisms underlying this risk amplification, including potential subtherapeutic drug levels or delayed immune response modulation.

Standardized penicillin regimens

The WHO-recommended benzathine penicillin G regimen (3 weekly 2.4-million-unit doses) reduced congenital syphilis incidence to 1.2% in the cohort, aligning with global benchmarks (e.g., 1.5% in Brazil [11]). Among high-titer cases (TRUST ≥ 1:16; n = 182), 51.6% (n = 94) achieved this serological threshold post-treatment (Figure 1), correlating with significantly reduced composite adverse outcomes (10.6% vs. 46.6%; $p < 0.001$). These findings underscore the critical imperative for universal implementation of antenatal screening and treatment protocols [12].

Socioeconomic and clinical drivers of success

Marital stability and education level emerged as independent predictors of treatment adherence. This parallels findings from sub-Saharan Africa, where socioeconomic barriers significantly impact syphilis management [13]. The importance of timely intervention is underscored by studies documenting that gaps in prenatal care and treatment lead to preventable congenital syphilis cases [4]. Early diagnosis (< 20 weeks gestation) and protocol adherence were critical, as delayed treatment (> 28 weeks) increased adverse outcomes by 4.2-fold (95% CI 2.1–8.3).

Limitations and future directions

Intrauterine *T. pallidum* exposure predisposes to small-for-gestational-age (SGA) infants (birth weight < 10^{th} percentile; 22.4% in our cohort) and neurodevelopmental impairment [14]. Our standardized follow-up protocol (0–36 months) mandates neonatal evaluation (cerebrospinal fluid-Venereal Disease Research Laboratory (CSF-VDRL), long-bone radiography, ophthalmoscopy), developmental monitoring (Bayley scales of infant development-III at 6/12/24 months), neuroimaging (brain magnetic resonance imaging (MRI) for microcephaly (head circumference ≤ 2 SD (In the context of anthropometric measurements, expressing a value (e.g., head circumference) in terms of standard deviations (SDs) from the population mean allows for the normalization of data across different ages and genders. A value that is ⩽ -2 SDs from the mean of an appropriate reference population falls at approximately the 23rd percentile, indicating a statistically significant deviation from the norm) or abnormal neurology).

Despite the efficacy of standardized treatment, residual adverse outcomes in seroresponsive cases (10.6%) may indicate underlying subclinical pathology, necessitating future studies to incorporate placental histopathology and longitudinal neurodevelopmental assessments for mechanistic clarification.

This study has several limitations inherent to its observational design. First, the lack of randomization introduces the potential for unmeasured confounding and selection bias, which may influence the observed associations between predictors (e.g., marital stability, education) and outcomes. Second, the analysis was constrained by data availability; specifically, we lacked information on critical confounders such as maternal HIV co-infection status, episodes of syphilis reinfection during pregnancy, and detailed socioeconomic factors. The absence of these variables limits our ability to fully adjust the risk estimates and may affect the generalizability of the findings. Despite these constraints, the study provides valuable real-world evidence on treatment timing and outcomes in congenital syphilis management.

Conclusions

Accurate diagnosis, timely intervention, and standardized management during early pregnancy are essential for improving the cure rate among pregnant women with syphilis and reducing the risk of adverse pregnancy outcomes. In the case of pregnant patients with syphilis, the same stringent and effective treatment criteria should be applied. In instances where high titers of TRUST are initially diagnosed during pregnancy, the absence of a response to treatment can serve as a reliable indicator for monitoring the risk of adverse pregnancy outcomes. While this study leveraged a robust cohort of 2,229 syphilis-complicated pregnancies to validate standardized penicillin regimens, the subgroup of women with initial high-titer TRUST (≥ 1:16) was relatively modest (n = 182), potentially limiting statistical power for rare outcomes in this high-risk population. Future multicenter studies with enriched high-titer samples are needed to confirm these findings and explore intergenerational health impacts.

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Authors' contributions

XL: conceptualization, methodology, data curation, formal analysis, writing—original draft preparation, writing—reviewing and editing; YJ: conceptualization, methodology, data curation, formal analysis, writing—reviewing and editing, supervision.

Corresponding author

Ji Yan, MD.
Taizhou Central Hospital, No. 199 Zhigu Road, Jiazhi Street, Jiaojiang District,
Taizhou City, Zhejiang Province, China.
Tel: 13967612161
Email: jiyan0402@163.com

Conflict of interest

No conflict of interest is declared.

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Annex – Supplementary Items

Case Reports illustration

Case 1 involved a small-for-gestational-age infant born at 38^{+6} weeks weighing 2,260 g. The maternal TRUST titer was 1:32. The initial neonatal serology showed a TRUST titer of 1:1 with TPPA positivity. Following intervention with benzathine penicillin G (50,000 U/kg), the infant's TRUST titer rebounded to 1:8 at 3 months, confirming congenital syphilis. A developmental quotient (DQ) of 75 at 6 months indicated initial developmental delay; however, this improved to a DQ of 89 after targeted rehabilitation.
Case 2 was a preterm neonate born at 33^{+6} weeks weighing 2,150 g, with both maternal and neonatal TRUST titers at 1:256 and TPPA positivity. Clinical signs included generalized bullae at birth. Outcomes included persistent TPPA positivity at 20 months, alongside microcephaly (-2.2 SD) and language delay, as reflected by a Griffiths General Quotient (GQ) of 78.
Case 3 was a term, small-for-gestational-age infant (2,260 g) whose TRUST titer rose from 1:1 to 1:8. This infant showed global developmental delay (DQ = 75) at 6 months. With early rehabilitation, the developmental quotient improved to 89 by 24 months.
Case 4 was a preterm infant (2,150 g) with a TRUST titer of 1:256. Despite treatment, the infant exhibited persistent microcephaly (-2.2 SD). A Griffiths assessment at 20 months revealed a specific language delay (GQ = 78), for which the infant benefited from subsequent speech therapy.