Original Article

Prevalence of Incomplete Post-Treatment Follow-Up Visits in Female Patients with Syphilis and the Associating Factors

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Background: Syphilis requires a simple treatment but long-term follow-up because of the frequent re-infection. However, data regarding this issue remains limited.

Objective: To demonstrate the prevalence of incomplete follow-up visits in Thai heterosexual women who were diagnosed with syphilis and its associating factors.

Materials and Methods: The cross-sectional study was conducted by reviewing all medical charts of patients with syphilis at the Siriraj Female STI Clinic between 2012 and 2017. Eligibility criteria included Thai, heterosexual women 60 years or younger, no human immunodeficiency virus (HIV) infection, and no cancer. Venereal disease research laboratory (VDRL), as the serological follow-up test, was routinely done at 3, 6, 9, 12, 18, and 24 months after the treatment unless re-infection occurred. Incomplete follow-up was defined as that the patient came to the clinic for less than six months after completing treatment.

Results: There were 215 eligible patients with an average age of 25-year-old. One hundred twenty-eight (59.5%) had incomplete follow-up visits and 30 (14.0%) had not a single follow-up. The number of follow-up visits was 0 to 8 times (median=1) and the follow-up time period was 0 to 41 months (median=3). The diagnosis included primary syphilis (7/215, 3.3%), secondary syphilis (16/215, 7.4%), early latent syphilis (8/215, 3.7%), and late latent syphilis (184/215, 85.6%). Of them, 131 (60.9%) were pregnant. The associating factors with incomplete follow-up visits were age of 19 years or younger, lower education than primary school, and living in a nuclear family (OR 0.49, 95% CI 0.28 to 0.88; 1.29, 95% CI 1.04 to 1.61; and 1.41, 95% CI 1.06 to 1.89).

Conclusion: Over half of Thai heterosexual women with syphilis had incomplete follow-up visits. The associating factors include age of 19 years or younger, lower education than primary school, and living in a nuclear family.

Keywords: Associating factors, Post-treatment follow-up visits, Syphilis

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Syphilis has always been one of the most concerned sexually transmitted infections (STIs) all over the world[1], including Thailand[2], because of its aggressive nature. It is caused by *Treponemal pallidum* subspecies *pallidum* bacteria, which can spread throughout the whole body, due to its drill-like shape and immune-avoidance surface[3]. The disease has been thoroughly studied resulting in accurate diagnostic methods and clear staging[4]. Penicillin is the antibiotic of choice for treating syphilis owing to its high efficacy and low incidence of drug resistance[5]. Despite that, post-treatment follow-up remains pivotal because this population is at risk for re-infection. Additionally, partner notification and treatment may be incomplete. The treatment guideline provided by the Center for Disease Control and Prevention (CDC) recommend post-treatment follow-up visits to up to at least 6 to 12 months[5].

Non-treponemal serological test, either venereal disease research laboratory (VDRL) or rapid plasma reagin (RPR), is the main tool during follow-up

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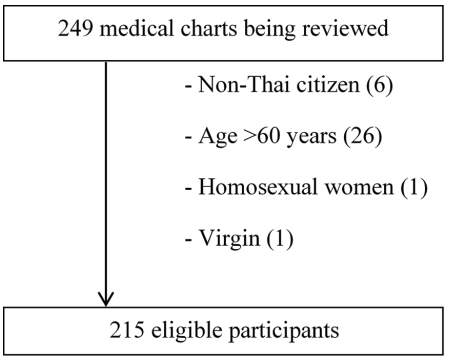

Figure 1. Flow of participants.

period as it varies with the activity of disease. Among syphilis patients without having human immunodeficiency virus (HIV), the decline of the non-treponemal serological titer of four folds or more at 6 to 12 post-treatment months is expected[5]. At the Siriraj Female STI Clinic, each patient receives an intensive, educational session for each visit to raise the awareness regarding safe sex practice and the whole follow-up schedule that includes 3, 6, 9, 12, 18, and 24 months. In addition, all sexual partners are welcomed to get blood tested and education. Our previous report showed that all male partners of women with syphilis came for serological evaluation at the clinic[6]. To mitigate the incomplete post-treatment follow-up visits, the present study aims to demonstrate its prevalence and associating factors.

Materials and Methods

After being approved by the Siriraj Institutional Review Board (COA No.Si105/2019), the chart review study was conducted at the Siriraj Female STI Clinic. All medical files recorded as "syphilis" cases between 2012 and 2017 were reviewed. The inclusion criteria were being Thai, heterosexual, younger than 60 years, and having no immunocompromised conditions such as HIV infection as it affects the response[7].

Participants

All women who were diagnosed with syphilis in Siriraj Hospital were sent to the Siriraj Female STI Clinic. They mainly came from the screening at the blood bank, antenatal care (ANC), and pre-operative unit. The main treatment modality was antibiotics, in accordance to the 2015 CDC guideline[5]. After completing the treatment protocol, all patients were asked to get 'VDRL' blood test at 3, 6, 9, 12, 18, 24 months, and yearly thereafter. All of the approachable sex partners were asked to receive blood screening using both treponemal and non-treponemal test. All infected partners were treated or contacted until the treatment was completed.

Outcome measures

Characteristics of all eligible participants were retrieved, including demographic data, obstetrical data, and history relating to STIs. Complete treatment was referred to giving all planned treatment protocol, especially that for late syphilis, which requires three doses of benzathine penicillin or 28 days of oral antibiotics[5]. Incomplete post-treatment follow-up was defined as having less than six months of visit at the Siriraj Female STI Clinic. Treatment failure is defined as VDRL titer declines less than four folds at six months[8]. However, in late syphilis, if the initial VDRL titer was low, this definition could not be applied. The persistent low VDRL titer at 12 months post-treatment was called "serofast". Data on partner treatment was derived from asking the indexed patients.

Statistical analysis and sample size calculation

Stata, version 12.1 (StataCorp LP, College Station, TX, USA) was used for the statistical analysis. Descriptive statistics were used to describe the characteristics of the participants. Minimum-maximum (min-max) and interquartile range (IQR) were used to describe non-parametric variables. Chi-square was used to compare categorical data. Student t-test and Wilcoxon rank-sum test were used to compare parametric and non-parametric continuous data respectively. Univariate logistic regression was used to demonstrate the associating factors with incomplete post-treatment follow-up visits. Statistical significance was defined as p-value less than 0.05.

Sample size calculation was done using the formula of prevalence. Based on our previous report that 61.4% of female patients being diagnosed with syphilis had less than six months of follow-up visits[9], the required sample size was 186 when the error was set at 0.05.

Results

Of the 249 reviewed medical charts, there were 215 eligible participants (Figure 1). The participants were around 25 years old. Most were high-school finishers. One-third were regular employees while another one-third were unemployed. The diagnosis included primary syphilis (7/215, 3.3%), secondary syphilis (16/215, 7.4%), early latent syphilis (8/215,

Table 1. Demographic data and sexual health history of women with syphilis (n=215)

	Total (n=215) n (%)
Age (year); mean±SD	23.6±8.7
Education	
None/primary school	53 (24.7)
High school	144 (67.0)
Bachelor degree or more	18 (8.3)
Occupation	
Housewife/unemployed	89 (41.4)
Temporary job	72 (33.5)
Regular incomer	31 (14.4)
Student	23 (10.7)
Nuclear family*	152 (70.7)
Sexual risk behaviors	
Sex debut (year); mean±SD	17.2±2.9
No. of lifetime partners; median (IQR), min-max	3 (2 to 6), 1 to 40
Anal intercourse	11 (5.1)
Oral intercourse	39 (18.1)
History of STIs	23 (10.7)
Obstetric history	
Being pregnant	131 (60.9)
GA (weeks) (n=131); mean±SD	17.9±8.1
Abortion; median (IQR), min-max	0 (0 to 0), 0 to 5
Parity; median (IQR), min-max	0 (0 to 1), 0 to 4
Syphilis history	
Symptomatic presentation	15 (7.0)
VDRL ≥1:8 before treatment	132 (61.4)
First time syphilis	203 (94.4)
Complete partner treatment	127 (59.1)

GA=gestational age; STIs=sexually transmitted infections; VDRL=venereal disease research laboratory; SD=standard deviation; IQR=interquartile range

* Nuclear family: living alone or not living with parents/guardians

3.7%), and late latent syphilis (184/215, 85.6%). Two hundred three out of 215 (94.4%) experienced the disease for the first time. Penicillin was used as the main treatment regimen (205/215, 95.3%). The treatment was completed at Siriraj Hospital in 204 out of 215 (94.9%) patients. Around 70% had regular partners and almost all had one current partner. They started having sexual relation at the age of 17 years. Approximately 10% had a history of STIs (Table 1).

Of them, 128 women (59.5%) had less than six months post-treatment follow-up visits and 30 (14%) had not a single follow-up. The median follow-up visit was 1 (min-max 0 to 8, IQR 0 to 3) and the median follow-up time period was three months (min-max 0 to 41, IQR 0 to 9). At 6-month follow-up 45/87 (51.7%) achieved a four-folds or better decline of VDRL titer. At 12-month follow-up, 21/52 (40.4%) had a successful treatment, 25/52 (48.0%) had serofast, and 6/52 (11.5%) were re-infected.

The comparison of demographic data and sexual health risks showed that participants with incomplete follow-up visits tended to be younger, had lower educational levels, living in a nuclear family had VDRL titer of 1:8 or greater before commencing treatment, and had incomplete partner treatment ($p<0.05$ for all) (Table 2). Table 3 shows the associating factors with incomplete post-syphilis treatment, which were age 19 years or younger, lower education than primary school, and living in a nuclear family (OR 0.49, 95% CI 0.28 to 0.88; 1.29, 95% CI 1.04 to 1.61; and 1.41, 95% CI 1.06 to 1.89, $p<0.05$ for all).

Discussion

Serological follow-up after commencing antibiotics is a crucial part of the syphilis treatment but over half of Thai female patients fail to comply with the schedule. While all of them receive an intensive educational session on each visit, more proactive strategies may be needed. The present study shows that young people are likely to have incomplete follow-up visits. Therefore, social network, which is popular in this population, may be a good tool to accomplish our goal[10]. Smart phones are affordable for everyone regardless of educational level or income. Therefore, information can be directly sent to individual patient at any time via social media applications.

Teenage population has been the focus group of Thai national health policy for the high incidence of unplanned pregnancy and STIs. Short movies regarding the outcomes of unprotected intercourse have been launched on the freely accessible programs. Moreover, sex education in schools is enhanced. Since 2014, the Siriraj Female STI Clinic has provided free educational media on internet and free consultation via electronic mail. Our next step is to promote an on-line communication for individual patient and promote a multidisciplinary care team for more holistic approach such as an involvement of social welfare.

Socioeconomic status does affect the personal health concern. As seen in the present study, living in a nuclear family is another associating factor of

Table 2. Comparison demographic data and sexual health history of women with syphilis between those with incomplete (<6months) and complete (≥6 months) post-treatment follow-up visits

	Follow-up visits <6 months (n=128) n (%)	Follow-up visits ≥6 months (n=87) n (%)	p-value
Age (year); mean±SD	22.0±7.7	25.7±11.0	0.005
Education			0.026
None/primary school	38 (29.7)	15 (17.2)	
High school	85 (66.4)	59 (67.8)	
Bachelor degree or more	5 (3.9)	13 (15.0)	
Nuclear family*	99 (77.3)	53 (60.9)	0.040
Obstetric history			
Being pregnant	74 (57.8)	57 (65.5)	0.256
GA (weeks) (n=131); mean±SD	20.1±8.6	16.8±7.8	0.025
Syphilis history			
Symptomatic presentation	9 (7.0)	6 (6.9)	0.449
VDRL ≥1:8 before treatment	86 (67.2)	46 (52.9)	0.034
First time syphilis	121 (94.5)	82 (94.3)	0.962
Complete partner treatment	57 (44.5)	70 (80.5)	<0.001

GA=gestational age; VDRL=venereal disease research laboratory; SD=standard deviation

* Nuclear family: living alone or not living with parents/guardians

Table 3. Associating factors with incomplete post-syphilis treatment

	Follow-up visits <6 months (n=128) n (%)	Follow-up visits ≥6 months (n=87) n (%)	Crude odd ratio (95% CI)	p-value
Age ≤19 years	61 (47.7)	27 (31.0)	0.49 (0.28 to 0.88)	0.015
Education: no/primary school	38 (29.7)	15 (17.2)	1.29 (1.04 to 1.61)	0.037
Nuclear family*	99 (77.3)	53 (60.9)	1.41 (1.06 to 1.89)	0.009
Being pregnant	74 (57.8)	57 (65.5)	1.39 (0.79 to 2.44)	0.256
Symptomatic condition	9 (7.0)	6 (6.9)	0.98 (0.34 to 2.86)	0.449

CI=confidence interval

* Nuclear family: living alone or not living with parents/guardians

having incomplete post-treatment follow-up visits. In the past, Thai people used to live in an extended family of which the members can help one another in many ways such as lending money and taking care of children when their parents are away. To overcome this obstacle, our clinic has provided kids' space and flexible visiting time.

Those with incomplete follow-up visits tend to have onward transmission of syphilis. The present study shows that they have higher VDRL titers and a lower rate of complete treatment, both for themselves and their partners. This underlines the importance of the post-treatment follow-up. As it is known, VDRL titer represents the activities of syphilis in that high titer implies greater contagion. Although our previous report showed that all of the female patients with syphilis in our clinic reported only one current partner[6], the number of sexual partners can be underreported. All of the sexual partners can get evaluated or treated if only the index patient has enough awareness and concern.

The scarce data regarding this issue is the main strength of the present study. To eliminate this easily curable STI, understanding the reasons behind incomplete follow-up is important. The second strength is that the non-treponemal and treponemal antibody tests were performed in one standardized laboratory. The present study results in high reliability in detecting re-infection and failure of treatment. Last, although the present study is a retrospective chart

review study, data collection is quite complete owing to the long-time experience of the Siriraj Female STI Clinic. Generalizability of the present study seems to be the limitation as it represents only the Thai female patients living in Bangkok.

Conclusion

Over half of the Thai heterosexual women with syphilis had incomplete follow-up visits. The associating factors include age of 19 years or younger, lower education than primary school, and living in a nuclear family.

What is already known on this topic?

Syphilis is a highly contagious and penetrative disease that can permanently destroy many organs, including in-utero fetus. Despite its simple treatment modality to break the onward transmission, long-term follow-up, up to one year, is required and must be properly planned.

What this study adds?

More than half of female patients with syphilis have less than six months of post treatment follow-up visits. They are likely to be young, have low education, and live in a nuclear family. This knowledge may help health policy makers to better design appropriate approach to this population.

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Conflicts of interest

The authors declare no conflict of interest.

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