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OBSTETRICS

The Surge of Maternal and Congenital Syphilis in a Tertiary Care Center in Bangkok, Thailand

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ABSTRACT

Objectives: Globally, syphilis in pregnancies remains a significant health concern, because the infection results in numerous maternal and fetal complications. However, in Thailand, documented evidence regarding the disease in the mothers and their newborns is scarce. Therefore, we conducted the study to explore the disease's trends in the aforementioned populations.

Materials and Methods: A 10-year retrospective descriptive study (1st January 2006 – 31st December 2015) was conducted at King Chulalongkorn Memorial Hospital, Bangkok, Thailand. Hospital records of syphilis-infected pregnant women and their infants were extensively reviewed by 2 obstetricians and a neonatologist. Descriptive statistics was leveraged to present patient's demographic and syphilis-related data.

Results: The percentage of syphilis-infected pregnant women increased from 0.05% in 2006 to 0.5% in 2015. Following the same trend, the percentage of infants with proven or possible congenital syphilis rose from 0% in 2006 to 0.06% and 0.13% in 2015, respectively. Interestingly, teenage pregnant women were particularly affected by the disease in the recent years; the incidence escalated from 10% to 30%. There were 16.4% (n = 12) of infected pregnant women who did not receive treatment antenatally, half of them were asymptomatic with positive serologic results (CMIA+, RPR-, TPPA+ results).

Conclusion: This study adds new information regarding the surge of maternal and congenital syphilis cases particularly in young pregnant women. This update will help to increase the awareness of obstetricians regards to syphilis screening and treatment during pregnancy period. Moreover, it emphasizes the importance of medical personnel's' familiarity with the reverse syphilis screening algorithm before applying to clinical practice.

Keywords: syphilis, pregnancy, congenital infection.

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การเพิ่มขึ้นของมารดาที่ติดเชื้อซิฟิลิสในระหว่างการตั้งครรภ์และทารกที่ติดเชื้อแต่กำเนิด

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บทคัดย่อ

วัตถุประสงค์: *เพื่อศึกษาอัตราการติดเชื้อซิฟิลิสในมารดาระหว่างการตั้งครรภ์ และทารกที่มีการ ติดเชื้อซิฟิลิสแต่กำเนิด ในระยะเวลา 10 ปี ตั้งแต่ปี พ.ศ. 2549 ถึงปี พ.ศ. 2558 ที่โรงพยาบาลจุฬาลงกรณ์*

วัสดุและวิธีการ: *ผู้วิจัยทำการศึกษาแบบเก็บข้อมูลย้อนหลัง โดยเก็บข้อมูลจากเวชระเบียนของ หญิงตั้งครรภ์ที่มาคลอดที่โรงพยาบาลจุฬาลงกร์ ตั้งแต่วันที่ 1 มกราคม พ.ศ. 2549 ถึงวันที่ 31 ธันวาคม พ.ศ. 2558 เวชระเบียนของหญิงตั้งครรภ์ที่มีการติดเชื้อซิฟิลิสในระหว่างการตั้งครรภ์ และเวชระเบียนของทารกถูกทบทวนโดยสูติแพทย์ 2 ท่าน และแพทย์ผู้เชี่ยวชาญด้านทารก ปริกำเนิดจำนวน 1 ท่าน ผลการเก็บข้อมูลจะถูกนำเสนอโดยสถิติเชิงพรรณนา*

ผลการศึกษา: *อัตราการติดเชื้อซิฟิลิสของมารดาระหว่างการตั้งครรภ์เพิ่มขึ้นจากร้อยละ 0.05 ในปี พ.ศ. 2549 เป็นร้อยละ 0.5 ในปี พ.ศ. 2558 เช่นเดียวกันกับอัตราการติดเชื้อซิฟิลิสแต่กำเนิด ซึ่งเพิ่มจากไม่มีการติดเชื้อในปี พ.ศ. 2549 เป็นร้อยละ 0.06 ใน ปี พ.ศ. 2558 นอกจากนี้ ร้อยละของทารกที่น่าจะมีการติดเชื้อในปี พ.ศ. 2558 ยังมีจำนวนถึงร้อยละ 0.13 การศึกษาพบ ว่าในจำนวนของมารดาที่มีการติดเชื้อซิฟิลิสทั้งหมดพบเป็นมารดาวัยรุ่นถึงร้อยละ 30 นอกจากนี้ การศึกษายังพบว่าร้อยละ 16 ของมารดาที่ติดเชื้อทั้งหมดไม่ได้รับการรักษาในระหว่างการตั้งครรภ์ ซึ่งเกือบครึ่งของมารดาเหล่านี้ไม่มีอาการแสดงขณะตั้งครรภ์แต่มีผลเลือดที่ผิดปกติ (CMIA+, RPR-,TPPA+)*

สรุป: *จากการศึกษาพบว่ามีการเพิ่มขึ้นของอัตราการติดเชื้อซิฟิลิสของมารดาในระหว่างการตั้ง ครรภ์ และการติดเชื้อแต่กำเนิดของทารกโดยเฉพาะในมารดาวัยรุ่น จากผลการศึกษาจะช่วยเพิ่ม ความตระหนักเกี่ยวกับการเกิดโรคและการรักษาซิฟิลิสในระหว่างการตั้งครรภ์แก่สูติแพทย์ นอกจากนี้ผลการศึกษายังเน้นย้ำถึงความสำคัญในการทำความเข้าใจการตรวจคัดกรองซิฟิลิสด้วยวิธี reverse screening ก่อนจะนำมาปรับใช้ในทางคลินิก*

คำสำคัญ: *ซิฟิลิส, การตั้งครรภ์, การติดเชื้อแต่ปริกำเนิด*

Introduction

Despite the availability of effective and safe antibiotic regimens, syphilis remains an ineradicable sexually transmitted infection[1,2]. The disease is caused by a spirochete, Treponema pallidum which has affected the human race for more than half a century[3]. Globally, syphilis in pregnancies remains a significant health issue. In 2012, approximately 930,000 pregnant women worldwide were estimated to have syphilis[4]. This number rivals the number of HIV-infected pregnant women. If syphilis is left untreated during pregnancy, it can result in numerous adverse maternal outcomes; miscarriages, premature deliveries, low birth weights, stillbirths, congenital syphilis and neonatal deaths. Additionally, these outcomes incur public health burdens[5-7]. Fetuses can extract syphilis from their mothers at any stage of the disease; however, transmission most commonly occurs during the early stages which leads to fetal hepatic dysfunction, placentomegaly, hematologic abnormalities and eventually hydrops fetalis[8].

Unfortunately, in Thailand, documented evidence regarding maternal and congenital syphilis is scarce; therefore, we conducted this study to examine the disease's trends in a large referral center in Bangkok, Thailand in order to increase obstetricians' awareness of syphilis, the almost neglected maternal infection, to improve the screening coverage and treatment strategy during the pregnancy period.

Materials and Methods

This is a 10-year retrospective descriptive study conducted in a tertiary care center (King Chulalongkorn Memorial Hospital, KCMH) in Bangkok, Thailand. Electronic clinical records of women who were diagnosed with syphilis during current pregnancy and who delivered at KCMH between 1st January 2006 and 31st December 2015 were retrieved. Chart records of the potentially affected infants were also extracted from the hospital database. The study was approved by the institutional review board, the Faculty of Medicine, Chulalongkorn University.

All pregnant women who attended antenatal clinic at KCMH were evaluated for syphilis in the first and third trimesters using rapid plasma reagent (RPR) test until February 2011, after which the testing was substituted by the treponemal chemiluminescence immunoassay (CMIA) (ARCHITECT Syphilis TP, Abbott Laboratories, Abbott Park, Illinois, USA). Treponema pallidum particle agglutination (TP-PA) test was leveraged to confirm the diagnosis during both periods. Pregnant women who were diagnosed with syphilis received standard treatment according to sexually transmitted diseases treatment guidelines published by the Center for Diseases Control and Prevention (CDC), USA[9-11]. Neonatologists were well aware of the maternal conditions; therefore, the infants were treated with standard antibiotic regimens accordingly.

Diagnoses of maternal and congenital syphilis obtained from the hospital database was extensively reviewed by 2 experienced obstetricians and a neonatologist[9-11]. In addition, demographic, clinical and laboratory data of these pregnant women and their infants were collected.

Data was analyzed by IBM SPSS software version 22 (IBM Corp, Armonk, NY, USA). Patient's demographic and syphilis-related data were presented by descriptive statistics.

Results

A total number of 56,475 pregnant women delivered and 57,637 infants were born at KCMH between 2006 and 2014. Syphilis was diagnosed during current pregnancy in 73 pregnant women (0.13%). The mean age of the infected pregnant women was 27.7 years old (SD 8.3 years) and the median gestational age at the time of diagnosis was 18 weeks (range 6-40 weeks). There were 71 singletons, one set of twins and one set of triplets contributing to 76 infants born to the

infected pregnant women. Nine infants were proved to have congenital syphilis (0.016%). Maternal and infant characteristics are shown in Table 1 and Table 2, respectively.

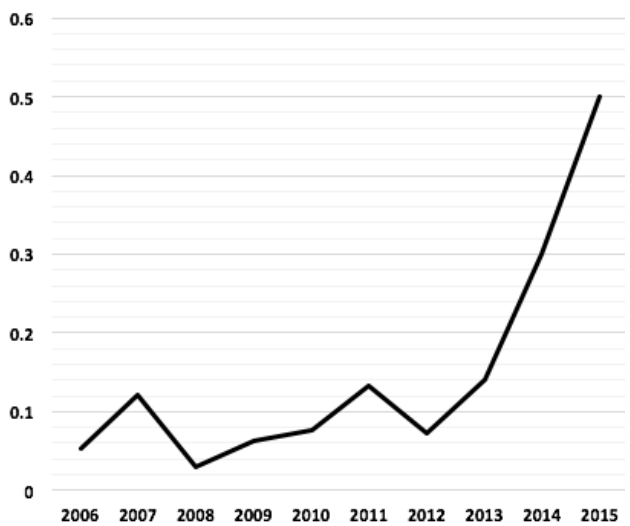
Between 2006 and 2014, the percentage of pregnant women identified as having syphilitic infection during current pregnancy had increased from 0.05% in 2006 to 0.50% in the final year (Fig. 1.). The percentage of infants with proven or possible congenital syphilis (Fig. 2.) also followed the same trend rising from 0% in 2006 to 0.06% and 0.13%, respectively, in 2015.

Table 1. Maternal characteristics.

Maternal characteristics	n=73 (%)
Gestational age at diagnosis	
• First trimester	24 (32.9)
• Second trimester	25 (34.2)
• Second trimester	24 (32.9)
Number of pregnancy	
• Primigravida	29 (39.7)
• Multiple gravida	44 (60.3)
Number of ANC	
• ≤ 4 times	22 (30.1)
• > 4 times	51 (69.9)
Maternal syphilis stage	
• Early syphilis (primary, secondary, early latent)	6 (8.2)
• Late latent/unknown duration	67 (91.8)
Maternal treatment regimen before delivery	
• None	12 (16.4)
• Benzathine penicillin G	57 (78.1)
• Ceftriaxone	3 (4.1)
• Erythromycin	1 (1.4)
Maternal co-infection	
• HIV	3 (4.1)
• Hepatitis B	1 (1.4)
Gestational age at delivery	
• < 37 weeks of gestation	17 (23.3)
• ≥ 37 weeks of gestation	56 (76.7)
Route of delivery	
• Vaginal delivery	53 (72.6)
• Cesarean delivery	20 (27.4)

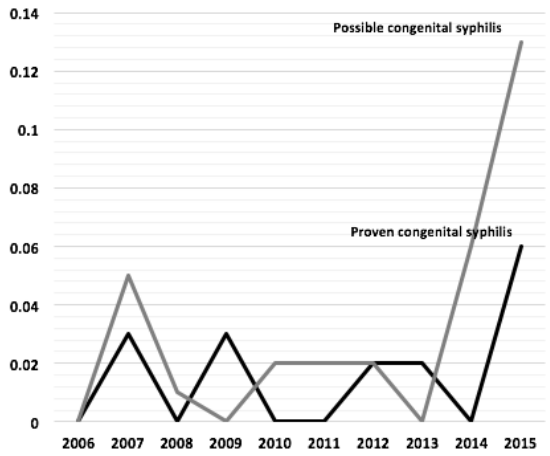
Table 2. Infant characteristics.

Infant characteristics	n=76 (%)
Birth weight	
• Very low birth weight	3 (3.9)
• Low birth weight	16 (21.1)
• Normal weight	57 (75.0)
Sex	
• Male	41 (53.9)
• Female	35 (46.1)
Syphilis related birth outcomes	
• Stillbirth	4 (5.3)
• Neonatal death	1 (1.3)
Infant syphilis status	
• Not infected	50 (65.8)
• Possible congenital infection	17 (22.4)
• Proven congenital infection	9 (11.8)



Year	Sypilis-infected pregnant women (total pregnant women = 56,475)	
	n	%
2006	3	0.053
2007	8	0.121
2008	2	0.030
2009	4	0.063
2010	3	0.077
2011	5	0.133
2012	4	0.073
2013	7	0.140
2014	14	0.300
2015	23	0.500

Fig. 1. Maternal syphilis.



Year	Proven congenital syphills		Possible congenital syphills	
	n	%	n	%
2006	0	0.00	0	0.00
2007	2	0.03	4	0.05
2008	0	0.00	1	0.01
2009	2	0.03	0	0.00
2010	0	0.00	1	0.02
2011	0	0.00	1	0.02
2012	1	0.02	1	0.02
2013	1	0.02	0	0.00
2014	0	0.00	3	0.06
2015	3	0.06	6	0.13

Fig. 2. Congenital syphilis.

Fig. 3. provides maternal age at the time of diagnosis divided into 2 different time periods; 2006-2010 and 2011-2015. Between 2006 and 2010, 10% (n=2) of the syphilis-infected pregnant women were younger than 20 years of age which escalated to 30% during 2011-2015. Notably, the percentage of early-stage syphilis cases also increased from 0% in 2006-2010 to 11.3% (n=6) in 2011-2015. Among women affected by early-stage syphilis, 83.3% (n=5) were under 25 years old.

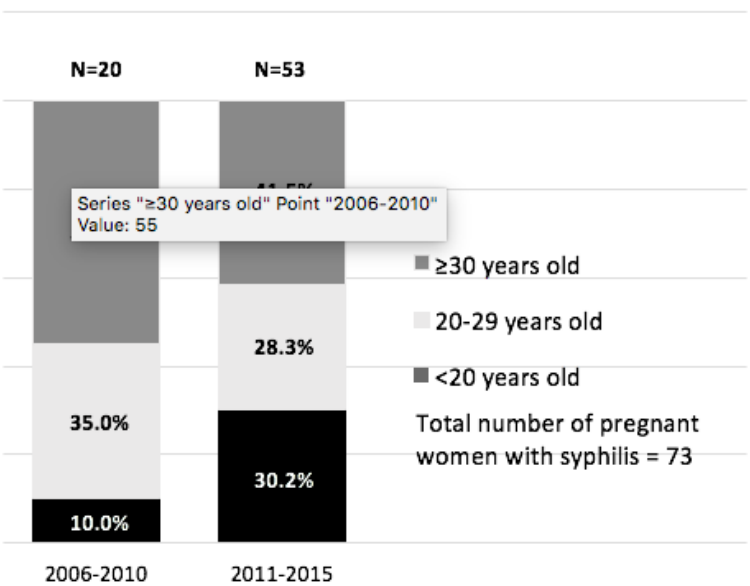


Fig. 3. Maternal age at diagnosis.

Overall, there were 16.4% (n=12) of infected pregnant women who did not receive any treatment before delivery. Table 3. provides clinical characteristics of untreated syphilis-infected pregnant women.

Of the 76 infants born to syphilis-infected pregnant women, 11.8% (n=9) of them were diagnosed with congenital syphilis. Out of the 9 affected infants, there were 7 singletons and one set of twins. Considering their maternal clinical characteristics, 55.6% (n=5) did not attend antenatal clinics and were newly diagnosed as having syphilis during intrapartum period. In addition, almost all of them (n=8) were diagnosed with syphilis in the third trimester and 77.8% (n=7) gave birth prematurely. The median interval from the diagnosis to delivery was 1 week (range 0-13 weeks).

Table 3. Diagnosis of untreated syphilis-infected pregnant women.

Diagnostic characteristic	n=12 (%)
Latent phase of unknown duration (CMIA+,RPR-,TPPA+)	5 (41.7%)
Diagnosis at delivery	4 (33.3%)
RPR: weekly reactive, TPPA+	3 (25.0%)

Discussion

According to our study, the percentages of pregnant women diagnosed with syphilis fluctuated around 0.1% during 2006-2013 which is well correlated with previous reports from Thailand and other Southeast Asia countries[4, 12, 13]. However, our recent data revealed that the number of syphilis-infected pregnant women had significantly increased for 2 consecutive years to 0.5% in 2015 which synchronizes with syphilis infection in particular population in the region; men who have sex with men[14, 15]. Not only did the number of infected pregnant women increase, but also the number of affected infants. The percentage of proven congenital syphilis cases remained stable between 0-0.03% during 2006-2014. Unfortunately, by the final year, the percentage sharply rose to 0.6%. In 2008-2009, previous study regarding congenital syphilis prevalence in Thailand unveiled that there were 0.1 case of congenital syphilis per 1,000 live births[16]. In consistent with the aforementioned study, we also demonstrated approximately similar incidence (0.01%) of congenital syphilis during the same period. However, we found a surge of congenital syphilis cases during the last 2 years.

In addition, we also discovered that during recent years, the number of syphilis-infected pregnant women who were younger than 20 years of age had increased from 10% to 30%. This trend correlates with other studies which evidence an escalating number of young women diagnosed with sexually transmitted diseases[17, 18]. Among syphilis-infected pregnant women who missed their treatment opportunities, majority of them were asymptomatic with positive serologic results as described; CMIA+, RPR-, TPPA+ results. This occurrence could be explained by the complicated interpretation of reverse syphilis screening algorithm as described by other studies[19-22]. Therefore, before applying the reverse syphilis screening algorithm, clinicians and medical personnels should be aware of and familiar with this approach.

With regards to congenital syphilis, in this study, nearly all infants were born to late presenters; pregnant women diagnosed in the third trimester or during delivery. Furthermore, a third of untreated women did not attend antenatal care. This finding emphasizes the importance of antenatal care in order to early detect any infection, to improve their health conditions and to prevent their infants from contracting the disease. As late treatment in third trimester, short interval between treatment initiation to delivery, preterm labor and inadequate antenatal care were

associated with syphilis-related adverse pregnancy outcomes and a greater number of congenital syphilis cases[23-25].

Conclusion

The strength of the study is that it adds new information with regards to the surge of maternal and congenital syphilis cases particularly in young adults. This updated insight will help increase the awareness of obstetricians regarding the importance of syphilis screening strategy and the treatment during pregnancy period. Timely identification of syphilis-infected women can substantially improve pregnancy outcomes, maternal health and prevent the infants from contracting the disease[26, 27]. However, the review was conducted in a single tertiary care center; therefore, further research is needed to confirm the rising trend of syphilis infection during pregnancy throughout the country.

Potential conflicts of interest

The authors declare no conflict of interest.

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