CSIRO PUBLISHING
Sexual Health, 2021, **18**, 197–199
https://doi.org/10.1071/SH21004

Letter to the Editor

Increase in congenital syphilis cases and challenges in prevention in Japan, 2016–2017

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Abstract. In Japan, the increase in congenital syphilis (CS) notifications has become a public health concern. We conducted a case series study to describe the characteristics of CS patients and their mothers. Of the 13 mothers who consented to participate, seven had regular prenatal care visits, including four who had tested negative at their first trimester syphilis screening. Only three mothers noted that their partners were tested, with all three partners being diagnosed with syphilis. Raising awareness for syphilis prevention during pregnancy, partner testing, and considering additional syphilis testing at the third trimester of pregnancy during times of increased syphilis prevalence is imperative.

Keywords: Asia, Japan, social determinants, surveillance, syphilis, women, partner testing, pregnancy, syphilis screening.

Received 4 January 2021, accepted 13 January 2021, published online 22 April 2021

Concomitant with the rise in syphilis in Japan,[1,2] congenital syphilis (CS) notifications have increased, from four cases (0.4 case per 100 000 live births) in 2012 to 14 cases (1.4 case per 100 000 live births) in 2016.[3] In response, we conducted a case series to identify key characteristics of CS patients and their mothers, along with challenges.[3] Eligible subjects were CS patients who were notified through national surveillance from March 2016 to October 2017 and their mothers. Information was collected using a questionnaire and face-to-face interviews with the patients' mothers and physicians (see[3] for methods).

Of the 17 CS patients notified, 13 of their mothers consented to participate. Nine were symptomatic, with a wide clinical spectrum at diagnosis (Table 1). The four asymptomatic CS patients were tested because their mothers had syphilis but had no or insufficient treatment during pregnancy. Most CS patients were tested by fluorescent treponemal antibody absorption (FTA-ABS) immunoglobulin M (IgM) antibody assay (Table 1), and 11/13 were treated with intravenous benzylpenicillin injection.

Common characteristics among the mothers were young age, unmarried, having a lower educational attainment, having other sexually transmissible infections (STIs), a history of commercial sex work, and no or inadequate prenatal care visits (Table 1). Three mothers who did not make any prenatal care visits were diagnosed with syphilis by a screening test at delivery. Three other mothers made visits irregularly, which prevented timely diagnosis. More than half (7/13), however, were making regular prenatal care visits. Four of these seven mothers tested negative at their first trimester test and were diagnosed after their infants' diagnosis of symptomatic CS; three experienced signs/symptoms of early syphilis (acute pharyngitis, severe itching and/or eczema) during pregnancy and consulted their respective physicians at the time but went

Table 1. Key sociodemographic and clinical characteristics of patients with CS and their mothers (n = 13)
RPR, rapid plasma reagin; PCR, polymerase chain reaction

Characteristics		*n* (%)	Remarks
CS patients			
Male sex		7 (54)	
Age at diagnosis	0 months	11 (85)	Two patients were diagnosed at 1 and 2 months of age respectively[A]
Clinical manifestation[B]		9 (69)	
Weeks' gestation		Median 35 (range 28–40)	Unknown for three patients
Birthweight		Median 2208 g (range 677–2956)	Unknown for one patient
Laboratory diagnosis method	FTA-ABS IgM antibody positive	8 (62)	
	FTA-ABS IgM antibody positive and infant serum RPR titer 4-folds higher than that of mother	3 (23)	
	Other	2 (15)	PCR-positive placenta (n = 1); serum RPR titer 2-folds higher than that of mother with untreated syphilis (n = 1, with clinical manifestations indicative of CS)
Vital status at investigation	Alive	13 (100)	Median age at time of investigation: 3 months (range 1–12)
Mothers			
Age (years)		Median 25 (range 18–40)	
Japanese nationality		12 (92)	Unknown for one mother
Unmarried		8 (62)	
History of commercial sex work		4 (31)	Unknown for two mothers
Receiving social welfare assistance		2 (15)	Unknown for two mothers
Highest level of education attained	High school	7 (54)	Unknown for five mothers
	University/Graduate school	1 (8)	
Prenatal care visit history	None	3 (23)	
	Irregular	3 (23)	First visit at second or third trimester
	Regular	7 (54)	
Presence of other STIs		5 (38)	*Chlamydia trachomatis* in four patients; *Chlamydia trachomatis* and *Neisseria gonorrhoeae* in one patient; unknown for four patients

[A]One patient born prematurely (36 weeks of gestation and 2120 g) was diagnosed after being noted with poor growth, rhinorrhea, and hepatosplenomegaly at the 1-month check-up visit. The other patient was full-term but developed hepatosplenomegaly, anemia, thrombocytopenia, and leukocytosis at 2 months of age; the physician initially suspected leukemia, but screening tests determined the cause as syphilis.
[B]Manifestations include hepatosplenomegaly, ascites, liver function abnormality, renal function abnormality, jaundice, anemia, thrombocytopenia, disseminated intravascular coagulation, purpura, elevated inflammatory response, hypoglycemia, persistent pulmonary hypertension, ventricular distention, and osteochondritis.

undiagnosed. The other three were those with a past syphilis diagnosis; though two tested positive for syphilis during the first trimester, CS was not prevented due to misdiagnosis as inactive syphilis or discontinuation of medication because of hyperemesis. Another was also initially diagnosed as past infection, but retesting during the third trimester indicated current, active infection. Regarding testing of sexual partner (s), only three mothers' partners were reportedly tested, with all three diagnosed with syphilis and two reportedly treated for syphilis.

In conclusion, while many mothers of CS patients had inadequate prenatal care visits as reported previously,[4–9] more than half of them had made routine visits, receiving a syphilis test at their first trimester. The four mothers who tested negative may have been infected during pregnancy; such events could have increased given the increased syphilis prevalence among heterosexuals.[1,10,11] Similar findings were recently reported from England and the US.[12,13] In addition, a mother was misdiagnosed with inactive syphilis; such 'false negative' diagnosis would also be expected to increase with higher syphilis prevalence (i.e. decrease in the negative predictive value of diagnosis).

During times of high syphilis prevalence, we emphasise the need for careful and sensitive diagnosis of syphilis in pregnant women. Clinicians should consider additional syphilis testing at the third trimester of pregnancy for high-risk women.[4,12,14] There is also a need to raise awareness for STI prevention among pregnant women, including partner testing. Inadequate communication regarding partner testing may have hindered timely diagnosis,[3,15] and healthcare providers could help facilitate communication. While challenges exist, our findings led to a multi-pronged response from the national

and local governments, together with the medical sector – updating of the national clinical guidance for syphilis, additional reporting requirements for surveillance, and development of locally-appropriate educational pamphlets. It is our hope that these approaches will contribute to CS prevention, both for the ongoing outbreak and any future re-emergence of syphilis.

Conflicts of interest

The authors declare that they have no conflicts of interest.

Declaration of funding

This study was supported by a grant from the Ministry of Health, Labour and Welfare of Japan (H27-Shinkou-Ippan-001).

Acknowledgements

Soichi Arakawa and Chie Jimbo are greatly appreciated for their administrative support. The authors thank all the physicians, mothers and infants who participated in this study. The authors greatly appreciate Masakazu Egashira, Takeshi Rikiishi, Noriko Nakayama, Hiroo Matsuo, Naoto Yamashita, Chisa Tsurisawa, Yuki Yamaguchi (Hagiwara), Akiko Kinumaki, Rina Okuno, Kazuki Miyabayashi, Yosuke Onoyama, and Shuhei Yamamoto for their assistance with the investigations and Eru Kozuki for discussions pertaining to surveillance of congenital syphilis. The authors also thank all the notifying physicians and the staff at local health centres and prefectural and municipal public health institutes who engage in surveillance activities in Japan.

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Handling Editor: Roy Chan