



## SCIENTIFIC LETTER

## Congenital syphilis on the rise. Review of a five-year period in a referral hospital in Portugal<sup>☆</sup>



### Sífilis congénita en aumento. Revisión de 5 años en un hospital de referencia en Portugal

Dear Editor,

There is evidence of a worldwide resurgence of syphilis, once nearly eradicated, and the subsequent risk for newborns. The 2022 European annual epidemiological report on congenital syphilis (CS) showed an increasing trend in the number of notified cases after 2020, and Portugal was one of the three countries with the highest incidence in both 2021 and 2022.<sup>1</sup> While European data for 2023 are still not available, the Minnesota Department of Health in the United States reported a 44% increase in the regional incidence of CS, with 29 notified cases—the highest in the past 40 years.<sup>2</sup> Worldwide, perinatal syphilis is the second leading cause of stillbirth and results in significant of morbidity and mortality.<sup>3</sup> Women with untreated early syphilis will pass the infection to 70%–100% of their offspring with the pregnancy ending in stillbirth in 1/3 of cases.<sup>3</sup> Vertical transmission occurs late in pregnancy (after 28 weeks), so early treatment of maternal syphilis infection using penicillin prevents fetal complications. In Portugal, pregnant women are screened for syphilis in every trimester with the venereal disease research laboratory (VDRL) test. Screening can also be performed in the delivery room if it was not performed in the third trimester or in the case of high risk or lack of prenatal care.

With the aim of determining the incidence of CS in Portugal, we conducted a retrospective study including children exposed to syphilis in utero and/or with congenital infection in the 2018–2022 period managed in a tertiary care hospital. We collected data on sociodemographic characteristics, maternal VDRL testing and newborn/child titers, coinfections,

birth records, maternal treatment during pregnancy, clinical features, treatment of the child and follow-up.

We present the cases of 9 babies born to mothers with syphilis infection. The cumulative incidence for this period was 0.0008% (9/10 731 deliveries), with an annual incidence of 0.0009%, 0.0009%, 0.0005%, 0.0005% and 0.001% from 2018 to 2022. **Table 1** summarizes the characteristics of the cohort. All mothers had positive VDRL titers. The maternal characteristics were as follows: 38 % (3) young mothers (age ≤ 25 years), 71% (5) had low educational attainment (elementary education), 57% (4) were unemployed, 22% (2) were from foreign countries (1 Guinean, 1 Brazilian), 11% (1) had coinfection by human immunodeficiency virus, 22% (2) had a history of substance abuse. Three out of seven (43%) mothers who received prenatal care were adequately treated. Maternal syphilis was classified as early in 56% (5), late in 33% (3) and undetermined in 11% (1). Seven newborns had positive VDRL titers. Of these cases, 22% (2) were classified as highly probable CS,<sup>4</sup> 67% (6) as possible CS<sup>4</sup> and 11% (1) as CS less likely.<sup>4</sup> There were two cases of early congenital syphilis, one of them manifesting as neurosyphilis. All patients were treated with parenteral penicillin G; 22% (2) were lost to follow-up and the remaining children have been healthy after treatment.

Although CS is a preventable disease, it continues to be a major global health problem, and its resurgence reflects deficiencies in prenatal care. Congenital syphilis still has a significant compound impact, and prevention should target specific maternal risk profiles, such as unstable housing, domestic violence, institutionalization, low socioeconomic status, high-risk sexual behavior, substance abuse etc. Shifts in global population demographics and distribution, including rising birth rates among foreign-born mothers in Portugal, could pose challenges to prenatal surveillance, which may affect the incidence of congenital infections. As is known, nearly 90% of syphilis infections occur in low-to-middle income countries (LMICs), with Africa bearing the most critical burden of CS at around 62%.<sup>5</sup> Nevertheless, syphilis rates in women of childbearing age have risen by more than 200% in high-income countries with a low incidence of congenital syphilis.<sup>6</sup> Further research is required to determine why CS prevention is failing. Applying a unified case definition, reinforcing surveillance, integrating syphilis screening in HIV testing and implementing disease registers could yield crucial data to enhance the management of CS and shape future interventions.<sup>6</sup>

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**Table 1** Clinical characteristics of the cases.

	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6	Case 7	Case 8	Case 9
Year	2018	2018	2019	2019	2020	2021	2022	2022	2022
Birth hospital	Inborn	Outborn	Inborn	Inborn	Outborn	Outborn	Inborn	Outborn	Outborn
Maternal age (years)	40	30	23	34	35	25	21	36	28
Level of education	Primary school	9 <sup>th</sup> grade	12 <sup>th</sup> grade	9 <sup>th</sup> grade	9 <sup>th</sup> grade	Unknown	12 <sup>th</sup> grade	9 <sup>th</sup> grade	Unknown
Nationality	Portuguese	Portuguese	Portuguese	Portuguese	Portuguese	Portuguese	Brazilian	Guinean	Portuguese
Risk factors	No	No	No	Institutionalized siblings	Institutionalized siblings, drug and alcohol abuse	No	No	Drug abuse, illegal immigrant	No
Prenatal care	No	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes
Coinfection	No	No	No	No	No	No	No	HIV	No
Classification of maternal syphilis	Undetermined	Late	Early	Late	Late	Early	Early	Early	Early
Probable trimester of infection	peripartum	3rd	2nd	2nd	peripartum	3rd	2 <sup>nd</sup>	3rd	1st
Treatment in pregnancy	No	No	Yes, inadequate	No	No	Yes, adequate	Yes, adequate	Yes, inadequate	Yes, adequate
Gestational age (weeks)	38	40	40	40	37	38	40	36	36
Birth weight (g)	3390	3690	2790	3150	2780	2905	3435	2510	2490
Presenting symptoms	No	No	No	No	No	Fever, poor weight gain, rash, jaundice, anemia, radiological bone abnormalities	No	Suspected epileptic seizures (not confirmed)	Pulmonary hypertension, anemia, thrombocytopenia, hepatosplenomegaly, liver function abnormalities
Long-bone radiographs	Normal	Normal	Normal	Normal	Unknown	Abnormal	Unknown	Normal	Normal
Maternal VDRL	1/1	1/64	1/16	1/1	1/1	1/512	1/64	1/32	1/128
Child VDRL	Negative	1/2	1/2	Unknown	Negative	1/32	1/1	1/8	1/32
Age at diagnosis (years)	Birth	4	Birth	Birth	Birth	Birth	Birth	Birth	Birth
Penicillin treatment (days)	10	10	10	10	Unknown	21	None (follow-up)	10	20
Outcome	Unknown	Healthy	Healthy	Healthy	Unknown	Healthy	Healthy	Healthy	Healthy

Thorough screening and treatment (including sexual partners) during antenatal/prenatal care is cost-effective and can decrease the incidence of CS, as evinced by the Chinese plan for the prevention of vertical transmission of syphilis in 2011, which reduced the incidence of CS from 91.6 to 11.9 cases per 100 000 live births.<sup>7</sup> In addition, we urgently need alternative antibiotics allowing shorter courses of treatment and oral administration to reduce the health care burden.<sup>6</sup> Overall, both public health interventions (attracting the attention of the media) and education of health care providers on the matter, namely the early detection of syphilis and its diagnosis and treatment, are warranted to curb this soaring health crisis.

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Sara Catarino<sup>a,\*</sup>, Lídia Carvalho<sup>b</sup>, Angélica Ramos<sup>b,c</sup>,  
Manuela Rodrigues<sup>d</sup>, Ana Reis-Melo<sup>e,f</sup>

<sup>a</sup> *Servicio de Pediatría, Centro Hospitalar Universitário de São João, Oporto, Portugal*

<sup>b</sup> *Servicio de Patología Clínica, Centro Hospitalar Universitário de São João, Oporto, Portugal*

<sup>c</sup> *Unidad de Investigación en Epidemiología (EPI), Instituto de Salud Pública, Universidad de Oporto, Oporto, Portugal*

<sup>d</sup> *Servicio de Neonatología, Centro Hospitalar Universitário de São João, Oporto, Portugal*

<sup>e</sup> *Unidad de Enfermedades Infecciosas e Inmunodeficiencias Pediátricas, Servicio de Pediatría, Centro Hospitalar Universitário de São João, Oporto, Portugal*

<sup>f</sup> *Departamento de Biomedicina, Facultad de Medicina, Universidad de Oporto, Oporto, Portugal*

\* Corresponding author.

E-mail address: [sara.ccat@gmail.com](mailto:sara.ccat@gmail.com) (S. Catarino).