European Journal of Obstetrics & Gynecology and Reproductive Biology 228 (2018) 274–278

Contents lists available at ScienceDirect

European Journal of Obstetrics & Gynecology and Reproductive Biology

journal homepage: www.elsevier.com/locate/ejogrb

Full length article

Features of syphilis seropositive pregnant women raising alarms in Hungary, 2013–2016

Eszter Balla[a,*], Gilbert G.G. Donders[b,c]

[a] Department of Bacteriology II., National Public Health Institute (former National Center for Epidemiology), Budapest, Hungary
[b] Femicare Clinical Research for Women, Tienen, Belgium
[c] Department of Obstetrics and Gynaecology, University Hospital Antwerp, Edegem, Belgium

ARTICLE INFO

Article history:
Received 5 June 2018
Accepted 20 July 2018
Available online xxx

Keywords:
Treponema pallidum
Syphilis
Pregnancy
Seroprevalence
Antenatal screening

ABSTRACT

Objectives: The incidence of syphilis has been on the rise in Hungary over the last decades. We aimed to assess the syphilis seroprevalence in pregnant women during 2013-2016. The secondary aims were to describe seropositivity by age and gestational age, to estimate infectivity rates in different age groups, and to compare the efficacy of mandatory prenatal screening versus individual venereological testing in revealing syphilis.

Study Design: During the above mentioned period the reactive serum samples (N = 527) of 49,965 pregnant women undergoing routine screening were submitted for syphilis verification to the Bacterial STI Reference Laboratory, National Center for Epidemiology, Budapest, Hungary. The confirmation process included titrated RPR and TPHA tests performed simultaneously. The tested women were considered seronegative if both tests gave negative results. When any of these tests proved indeterminate or positive, anti-Treponema pallidum IgG and IgM ELISA tests were performed. Patients confirmed for the presence for specific IgG were judged seropositive. Further evaluation of potential infectivity of seropositive patients was carried out on RPR reactivity.

Results: Syphilis seropositivity was detected in overall 2.9‰ (N = 148) of the cases. RPR-negative cases, i.e. past infections were confirmed in 36% (53/148); weak-reactive RPR (titres≤8) cases, i. e. past/early acute infections in 37% (55/148); strong-reactive RPR (titres>8) cases suggesting recent syphilis in 27% (40/148). Half of the infectious syphilis cases (20/40) belonged to the 15–24 age group. The gestational age at screening was available of 123 seropositive women, out of whom 27 (22%) were diagnosed late, in the third trimester. Nineteen (13%) out of all seropositives were detected via individual venereological testing before/instead of general prenatal screening.

Conclusions: The majority of infected pregnants may remain undetected due to the lack of mandatory general prenatal screening. The seropositivity for syphilis in pregnancy of 2.9/1000, of which one quarter were recent and infectious, the late diagnosis of syphilis in one in five, and the low pick-up rate of individualised instead of generalized screening are alarming signals and call for more effective prevention strategies, focusing on the most vulnerable adolescents, as well as on the first trimester of pregnancy.

Introduction

Based on 2007 estimates, *Treponema pallidum (T. pallidum)*, responsible for syphilis, infects more than 2 million pregnant women per year worldwide. If left untreated, it not only has serious consequences for the women, but also causes transplacental transmission with serious fetal/neonatal morbidity and mortality [1]. Being a fully preventable syndrome, the incidence of congenital syphilis is used as an indicator of the prevalence of infectious syphilis among the reproductive age population, and that of the efficiency of the prenatal health care system in general [2]. As both the screening methods and the adequate therapy are inexpensive, especially when compared to the enormous medical and socio-economic burden of the long-term health consequences of syphilis during gestation, antenatal screening for syphilis is either strongly recommended or is mandatory in most countries [2,3].

Besides geographic changes in epidemiology, several diagnostic pitfalls also affect the efficient recognition of maternal syphilis. Primary chancres frequently present in hidden anatomical sites

* Corresponding author at: 2013 Pomáz, Móricz Zs. u. 6/B, Hungary.
E-mail address: balla.eszter@oki.antsz.hu (E. Balla).

https://doi.org/10.1016/j.ejogrb.2018.07.022
0301-2115/

such as the vulva or perineum, and are not long-lasting and self-limiting. Due to the variable, often atypical presentations of secondary syphilitic mucosal or skin lesions, misdiagnosis is frequent. Finally, during the latent early or late phases of the infection the absence of symptoms may cause the failure to alert the clinician. A systematic antenatal serological screening, on the other hand, reveals infected mothers in almost all stages of *T. pallidum* infection, although it may remain a challenge to detect any (re)infection later in pregnancy after a first negative syphilis test during early pregnancy. For that reason, a repeated third trimester testing of initially negative women is recommended in some guidelines, especially in areas or subgroups known to have a high prevalence of syphilis [4].

A last drawback is that no single test is in itself fully optimal for an unequivocal laboratory diagnosis of syphilis. Hence a combination of various serological methods is recommended for proper screening and confirmation purposes [4,5].

All the socio-economic, pathologic and diagnostic features listed above contribute to the fact that maternal syphilis is still often underdiagnosed and underreported. Furthermore, some women, especially from the more vulnerable risk groups like adolescents, drug abusers or women from poor socio-economic situations, fail to present for routine antenatal follow-up tests [6]. However, these infected women may still be picked-up by opportunistic testing and via partner notification. Syphilis screening is regulated by a recommendation in Hungary, and ideally should be performed during the first prenatal visit. However, we still have no national data about the seropositivity rate among pregnant women in Hungary.

Therefore, the aim of this study was to determine the syphilis seroprevalence in a large group of pregnant women in Hungary during the period 2013-2016. Furthermore, we aim to assess the rate of infectious syphilis in different age and gestational age groups as well as to compare the efficacy of routine screening versus individual venereological testing in revealing syphilis during pregnancy.

Materials and methods

Samples, study population

From January 2013 to December 2016 the serum samples of 49,965 pregnant women were collected by physicians and sent for further syphilis screening, predominantly as a part of the routine prenatal care. The study population lived in the central area of Hungary (Budapest and the neighbouring counties). Large scale serum samples were tested with an automated ELISA system (Trepanostika TP, MicroELISA BioMérieux, France) for the presence of specific *T. pallidum* IgG/IgM antibodies (Table 1). All the prescreened samples showing reactivity (N = 527) were submitted for further verification to the Bacterial STI Reference Laboratory, National Center for Epidemiology, Budapest.

Table 1
Yearly distribution of number and rate of seropositive pregnant women/ prescreened women.

Year	Nr of prescreened pregnant women	Nr /rate of seropositive pregnant women	
2013	6 800	14	2‰
2014	11 560	32	2.7‰
2015	14 348	49	3.4‰
2016	17 257	53	3‰
ALL	49 965	148	2.9‰[a]

[a] Average prevalence value.

Laboratory methods

Confirmation included a titrated Rapid Plasma Reagin (RPR) test (Omega Diagnostics, Alva, Scotland) and a Treponema Pallidum Haemagglutination Assay (TPHA) (Trinity BioTech, Bray, Ireland). When both of these tests were found negative, the samples were judged negative and no further tests were performed as they had no serological sign of a past or an acute syphilis. When any of these tests were found indeterminate or positive, anti-*Treponema pallidum* IgG and IgM ELISA (Euroimmun, Lübeck, Germany) tests were performed. All women interpreted as syphilis seropositive had specific anti-Treponemal IgG detected by ELISA. The end-titres were also evaluated by a two-fold dilution method of the sera showing some RPR activity.

Results

One hundred and forty-eight women were seropositive (specific *T. pallidum*-IgG positive) during this 4-year period (global seroprevalence 2,9‰). Seroprevalence was 2‰ in 2013 (14/6800), 2.7‰ (32/11560) in 2014, 3.4‰ (49/14348) in 2015 and 3‰ (53/17257) in 2016 as shown in Table 1.

The potential infectivity of the seropositive samples was based on their RPR reactivity with a cut-off of higher than 1:8 dilution degree [6,7,8]. (Table 2.) RPR-negative cases indicative of a past infection were found in 53 (36%) of 148 women, while a weak reactive RPR (titers$\leq$ 1:8), referred to as either past or early active infection, was observed in 55 women (37%).

A strong RPR reactivity (titers >8), suggestive of a recent, infectious syphilis, was present in 40 (27%) of the 148 seropositive women. Half of the latter (20/40) belonged to the age group of 15–24 years, while we found 6 cases out of 40 suffering from active, infectious syphilis in the age group of 35 years or above.

The gestational age at sampling was reported in 123 of the 148 seropositive cases. Seropositivity was diagnosed in the second trimester in 56 of them (45.5%), and in the third trimester in 27 of them (22%). Of these 27 seropositive women 7 (26%) had serological evidence of recent, infectious syphilis (Table 3).

Of all the seropositive cases, 19 (13%) originated from random venereological investigation, while the majority of them, i.e. 129 (87%) were detected as a result of the routine general prenatal screening (Table 4). Venereological investigation meant in our series that women were referred for syphilis tests by venereologists (before a general prenatal screening could have been performed, or instead thereof) only due to contact tracing, i.e. as a consequence of the confirmed syphilis of their sexual partners.

Based on personal consultation data, all data in our study were first antenatal testing results, as no retesting occurred among the analysed seropositive group. So all the results discussed in this paper reflect the serostatus of the first screening in every pregnancy.

Table 2
Distribution of RPR titres in different age-groups of seropositive pregnants (N = 148).

	Age-groups (years)					
RPR result	15-19	20-24	25-29	30-34	35<	All
negative	4	10	7	12	20	53 (36%)
positive ≤8	11	15	13	6	10	55 (37%)
positive >8	6	14	7	7	6	40 (27%)
All	21	39	27	25	36	148