An eight-year retrospective analysis of antenatal screening results for syphilis: is it still cost effective?

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Abstract
Introduction: This study aimed to document the prevalence of syphilis among pregnant women in Turkey.
Methodology: In this retrospective cohort study, a total of 63,276 sera obtained between January 2007 and June 2014 from women who were routinely screened for syphilis as a part of antenatal care at a tertiary referral hospital in Turkey were analyzed. Serological screening was done with the rapid plasma reagin (RPR) test on venous blood samples. Treponema pallidum hemagglutination assay (TPHA) was the confirmation test for the diagnosis of syphilis in patients who had positive results in the screening test.
Results: Between 2007 and the first six months of 2014, 41 RPR+ and only five confirmed syphilis-positive patients were determined. The syphilis seroprevalence rate was 0.0648%. Within these years, there was no case of congenital syphilis detected in the hospital.
Conclusion: As there is evidence of effective screening of syphilis contributing to the effective treatment and prevention of adverse outcomes, routine antenatal screening of syphilis is recommended. The rationale depends on the consideration of the serious results of not treating the disease and the cost effectiveness of screening.

Key words: syphilis; prevalence; pregnancy; antenatal care.


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Introduction
Syphilis has remained one of the major public health problems, especially in developing countries. The World Health Organization (WHO) reported that more than two million pregnant women, mostly from low-income and middle-income countries, have active syphilis every year [1].

Treponema pallidum is able to cross through the placenta and infect the fetus from the sixth gestational week, and the transmission risk increases with time. Clinical manifestations are not apparent until 16 weeks of gestation, when fetal immunocompetence develops. Transmission may also occur during delivery [2-4].

Antenatal syphilis screening is highly recommended by reproductive healthcare programs [5]. The goal of antenatal screening for syphilis is primarily to detect pregnant women with congenitally transferrable syphilis. Congenital syphilis is a multi-organ infection resulting in stillbirth (24.7%), premature birth (24.7%), neonatal death (12.3%), severe illness in the infancy period (4.1%), and infant death (11.2%) [6-9]. Congenital syphilis can be prevented with early detection and adequate treatment [10].

Traditionally, congenital syphilis prevention relied on pregnancy screening of primary and secondary syphilis [11,12]. Importantly, the majority of women with syphilis are asymptomatic, and therefore serological screening is the only method of diagnosis. Treponema pallidum cannot be cultured. Also, identification of the spirochete is only possible in patients with lesions of primary or secondary syphilis [13]. Therefore, serologic testing is the preferred method to diagnose syphilis for screening purposes or in patients with suspected disease [8].

The Centers for Disease Control and Prevention (CDC) recommends universal serological syphilis screening during early pregnancy, which should be repeated in the third trimester and at delivery for populations where syphilis prevalence is high or patients are at high risk [14]. All women who experience stillbirth after 20 weeks of gestation should be tested for syphilis [14].

The present study aimed to determine the syphilis prevalence among patients attending the outpatient
Methodology

This was a retrospective cohort study based on patient records obtained from the outpatient clinic of the Zekai Tahir Burak Women Health Care, Training and Research Hospital in Ankara, Turkey. The institutional review board and the research ethics committee approved the study protocol. Serological syphilis screening was performed free of charge on all pregnant women as a part of routine antenatal care at their first hospital visit during pregnancy. During this period, 63,276 sera were obtained between 2007 and the first six months of 2014 for syphilis testing at the outpatient clinic of a tertiary referral center. Serological screening was performed using the rapid plasma reagin (RPR) test. Treponema pallidum hemagglutination assay (TPHA) was used to confirm positive screening results for syphilis for the diagnosis of patients with positive results [15]. Two technicians reviewed each result independently during the whole process.

The data were presented as number with percentage for categorical variables. SPSS (Statistical Package for the Social Sciences) version 21.0 was used for the statistical calculations. The data were summarized as mean ± standard deviation and median (minimum–maximum).

Results

Among 63,276 patients, the mean age was 26.5 years (range, 11–49 years). The incidence of positive syphilis serology was found to be 0.0648% (41 patients), and five confirmatory tests were positive (0.0079%). During the study period, there were 150,661 deliveries of 154,176 babies in the hospital. All five of the TPHA-positive pregnant women diagnosed with syphilis were treated with benzathine penicillin and all except one gave birth to normal babies without any signs of congenital syphilis. One pregnancy with a TPHA-positive pregnant patient is still in antenatal follow-up and is being treated (Table 1).

Discussion

Prevention of congenital syphilis with antenatal screening and treatment has been well established [16,17]. Our hospital is a tertiary healthcare referral institution that serves a population with a varied ethnic and socioeconomic base and is one of the biggest women’s health care centers in Turkey. We found that the prevalence of syphilis seropositivity was very low in our population. We determined only five confirmed syphilis cases among 63,276 pregnant women between January 2007 and June 2014 (0.0079%). The present report presents the data of the largest pregnant population from Turkey to date. Although in Turkey there is no health policy for screening for syphilis and there are different approaches among hospitals, in our hospital we routinely screen all patients at the first antenatal visit.

During the study interval, there was no newborn diagnosed with congenital syphilis. At the beginning of the study, we did not expect such a low prevalence of syphilis. It may be due to regional or socioeconomic characteristics of the population screened, but it is still important in order to discuss the cost effectiveness of antenatal syphilis screening because of the size of the study population.

There is a lack of population-based data regarding the exact prevalence of syphilis in Turkey. Aktürk et al. in their 2009 report referring to Ministry of Health

<table>
<thead>
<tr>
<th>Year</th>
<th>N</th>
<th>RPR+</th>
<th>%</th>
<th>TPHA+</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>2007</td>
<td>4,530</td>
<td>13</td>
<td>0.2870</td>
<td>1</td>
<td>0.0221</td>
</tr>
<tr>
<td>2008</td>
<td>5,990</td>
<td>13</td>
<td>0.2170</td>
<td>2</td>
<td>0.0334</td>
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<tr>
<td>2009</td>
<td>7,018</td>
<td>8</td>
<td>0.1140</td>
<td>0</td>
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<tr>
<td>2010</td>
<td>8,934</td>
<td>1</td>
<td>0.0112</td>
<td>0</td>
<td>0.0000</td>
</tr>
<tr>
<td>2011</td>
<td>10,645</td>
<td>2</td>
<td>0.0188</td>
<td>0</td>
<td>0.0000</td>
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<tr>
<td>2012</td>
<td>10,949</td>
<td>0</td>
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<td>0</td>
<td>0.0000</td>
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<tr>
<td>2013</td>
<td>10,905</td>
<td>1</td>
<td>0.0092</td>
<td>1</td>
<td>0.0092</td>
</tr>
<tr>
<td>2014</td>
<td>4,305</td>
<td>3</td>
<td>0.0697</td>
<td>1</td>
<td>0.0232</td>
</tr>
<tr>
<td>Total</td>
<td>63,276</td>
<td>41</td>
<td>0.0648</td>
<td>5</td>
<td>0.0079</td>
</tr>
</tbody>
</table>

RPR: rapid plasma reagin; TPHA: Treponema pallidum hemagglutination assay

Table 1. Seropositivity rates of syphilis over years
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2011 progress report on the global HIV/AIDs

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transmitting the disease perinatally to their unborn

nearly 1.4 million pregnant women had a probable

[15]. Estimates from the WHO in 2008 revealed that

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country, including men [18]. Dilek et al. evaluated

blood donors over a nine-year period for various infectious diseases, such hepatitis B, hepatitis

C, syphilis, and HIV seropositivity. Of the 39,002
donors, 16,601 (42%) were females. Although the

overall positivity rate of the Venereal Disease
Research Laboratory (VDRL) test was 0.057%, it was

not calculated for female donors separately [19]. Oner
et al. published a descriptive study conducted among

30,716 blood donors in the Mediterranean region of

Turkey. There were no positive VDRL results detected
among 1,129 female donors in the study [20]. There

are two studies from Turkey that provide syphilis
seropositivity rates of pregnant women; Demirel et al.
reported a seroprevalence of syphilis of 0.1% among

916 patients from the eastern region of Turkey [21],

and Nas et al. found only one VDRL+ patient among

3,050 pregnant women in 1999 but could not confirm
the diagnosis of syphilis [22]. According to these few
national publications focusing on prevalence
determination, although Turkey takes its place among

the countries with a very low prevalence of syphilis,
this may not remain so indefinitely. This issue may be
a reason for discussing the cost effectiveness of
syphilis screening in Turkey.

Congenital syphilis is now rare in wealthy
countries; however, adverse pregnancy outcome
results are still important public health problems in
many underdeveloped or developing areas. In 1993,
the World Development Report first determined that
syphilis screening during the antenatal period is one of
the most cost-effective actions that can be taken to
improve children’s health [23]. The WHO states that
the biggest problem is inadequate screening of syphilis
in regions where the infection has a higher prevalence
[23]. A WHO initiative to eliminate mother-to-child
transmission of syphilis aims for a ≥ 90% pregnant
women screening rate and to provide adequate
treatment for ≥ 90% of seropositive women by 2015
[15]. Estimates from the WHO in 2008 revealed that
nearly 1.4 million pregnant women had a probable
active syphilis infection and were at risk of
transmitting the disease perinatally to their unborn
children [24]. Despite highly recommended preventive
health care programs, one-third of women are not
tested for syphilis during antenatal care management,
and a large number in the population will remain
untreated [24,25]. In the WHO/UNAIDS/UNICEF
2011 progress report on the global HIV/AIDS
response, low- and middle-income countries reported
syphilis testing as part of antenatal care (ANC) in 68%
of women; however, this number may not reflect the
most objective findings because of the lack of an
organized reporting system [26]. In the present report,
there was no available data from Turkey concerning
the proportion of women attending ANC who were
screened for syphilis at the initial visit. We believe that
the data of 63,276 pregnant patients reflects a large
population and provides important information.

Access to antenatal care is one of the agreed
milestones of progress towards the Millennium
Development Goals (MDG). Infections, as well as
prematurity and birth asphyxia, contribute to 80% of
neonatal deaths, and it has been shown that improving
healthcare programs (including syphilis screening)
beginning from the antenatal period would avert
neonatal and infant deaths in order to attain the fourth
MDG [27,28]. For the worldwide elimination of
mother-to-child transmission of syphilis, one of the
important steps defined in the report was “early
antenatal care”; which was found in a meta-analyses to
decrease adverse pregnancy outcomes caused by
syphilis infection of the mother when compared to
pregnant women seen at the third trimester (odds ratio,
2.24) [29]. In some countries where seropositivity
prevalence rates of syphilis are high or new
seroconversion cases are detected during ongoing
pregnancies, and where the population is composed of
various ethnic and social characteristics, revision of
the screening protocol is a question for antenatal care
management policies. Some countries, especially in
Europe, which are targets of migration flow, are also
subject to a rise in the prevalence of syphilis. In these
countries, applying a second screening test in the last
trimester of pregnancy has been proposed [30].

Studies aiming to determine the most optimal test
for syphilis are still in progress. There are two
commonly used serological tests for syphilis: the
non-
treponemal and the treponemal tests. Serologic
screening with a non-treponemal test is used to
identify patients with possible untreated syphilis
infection. To date, non-treponemal tests are in use that
have acceptable accuracy, sensitivity, and cost [31].
Non-treponemal tests are the VDRL and RPR tests.
These tests are relatively inexpensive and sensitive
(86%–100% for RPR and 78%–100% for VDRL),
making them useful as screening tests, but they require
at least a basic laboratory. A positive screening test is
confirmed by one of the treponemal tests: TPHA,
fluorescent-treponemal antibody-absorbed test (FTA-
ABS), and microhemagglutination test for antibodies
to T. pallidum (MHA-TP). TPHA and enzyme
immunoassays (EIA) are more expensive and require

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a reference laboratory [14]. The rate of false-positive results is lower in treponemal tests than in non-treponemal tests. Previous studies have demonstrated that several conditions, such as tumors, infectious diseases, and autoimmune diseases can cause biological false-positive (BFP) reactivity. Also, elderly people and pregnant women are at risk of false-positive results because of higher autoantibody titers [32,33].

Many studies calculating the cost effectiveness of screening compared to costs of treating infants with congenital syphilis, severe adverse outcomes, and disability-adjusted life years (DALY), found that antenatal screening of syphilis is highly cost effective, even in areas with very low prevalence rates [34-36]. When positive-screened pregnant women are treated adequately, the effectiveness of treatment is assumed to be 100% for prevention of adverse outcomes. This high rate of cure after treatment makes the decision to take action in public health policies very easy.

Conclusions

Since there is evidence of effective screening of syphilis contributing to the effective treatment and prevention of adverse outcomes during pregnancy, such as severe illness in the infancy period and perinatal death, and given the acceptable costs of screening tests, routine antenatal screening for syphilis is suggested. The rationale depends on the comparison of the serious results of not treating and the cost effectiveness of screening.

References


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