Congenital Syphilis Surveillance and Newborn Evaluation in a Low-Incidence State

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Objectives: To evaluate congenital syphilis surveillance in Minnesota, to assess the evaluation and management of newborns at risk for congenital syphilis, and to assess prenatal syphilis screening.

Design: Case ascertainment and medical record review.

Setting: The 7-county Minneapolis-St Paul metropolitan area.


Main Outcome Measures: The completeness of congenital syphilis case ascertainment, maternal demographic data, maternal syphilis management, newborn evaluation for and management of congenital syphilis, and hospital syphilis screening practices at delivery.

Results: Eighty mother-infant pairs who were at risk for congenital syphilis were identified from 3 sources. Using the Centers for Disease Control and Prevention's congenital syphilis case definition, 36 infants (45%) were classified as probable cases, 42 (53%) were classified as noncases, and 2 (3%) were syphilitic stillbirths. Forty-seven women (59%) had syphilis serologic tests performed in the third trimester; only 37 (46%) had syphilis screening at delivery. Conditions of the mothers of 8 probable cases (22%) were diagnosed at delivery. Most probable cases (86%) were evaluated; only 56% were evaluated adequately. Twenty-five probable cases (69%) were treated. Most hospitals did not have formal policies for syphilis screening at delivery. The Minnesota Department of Health's congenital syphilis registry lacked sensitivity (39%) as a case ascertainment method.

Conclusions: Clinicians should adhere to standardized protocols in the evaluation and management of at-risk newborns. Vigilant screening prenatally and at delivery and adequate follow-up are critical to reduce congenital syphilis. Improved surveillance data and resources are needed for the identification and follow-up of newborns at risk for congenital syphilis.

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ESPEDE available and effective treatment for syphilis, congenital syphilis remains a public health and clinical challenge. After 2 decades of declining rates of primary and secondary syphilis, the incidence of early syphilis and congenital syphilis increased markedly in the 1980s and early 1990s.1,2 Although some of the reported increase in congenital syphilis was attributable to the Centers for Disease Control and Prevention's (CDC's) expansion of the surveillance case definition for congenital syphilis in 1988,3 a true increase is suggested by the epidemic of early syphilis in women of childbearing age.1,2 Although the incidence of syphilis in Minnesota is lower than the national rate, similar temporal trends have occurred here, with higher rates observed in urban areas (Figure).4 Although the syphilis epidemic has diminished during the past 5 years and the national incidence rate (3.2 cases per 100000 population) is at an all-time low,5 syphilis remains a significant endemic public health problem. Furthermore, periodic epidemics will continue to occur until syphilis is eliminated.6

In a low-incidence state such as Minnesota, evaluation and management of newborns at risk for congenital syphilis are particular challenges for health care providers. The CDC surveillance definition, which was revised in 1996, is highly sensitive and often includes asymptomatic infants.1,8 Also, clinicians caring for newborns often are unfamiliar with the complex protocols for evaluation and management of congenital syphilis. In addition to the CDC's surveillance case deli-
METHODS

In Minnesota, health care practitioners and laboratories are required to report syphilis cases to the Minnesota Department of Health (MDH). Infants possibly at risk for congenital syphilis and born in the 7-county Minneapolis–St Paul metropolitan area during 1992 through 1994 were identified from 3 sources: (1) the MDH’s congenital syphilis registry, (2) discharge records from hospitals in the metropolitan area for infants younger than 2 years with an International Classification of Diseases, Ninth Revision (ICD-9) discharge diagnosis code consistent with congenital syphilis during the study period, and (3) pregnant women who were diagnosed as having syphilis and reported to the MDH in 1991 through 1994 and who had delivered during 1992 through 1994. Eligible mother-infant pairs included those in which the mother had a history of syphilis during pregnancy and/or the newborn was diagnosed as having congenital syphilis during the study period. This study was approved by the Human Subjects Review Committee at Hennepin County Medical Center.

Hospital records for all mothers and newborns identified were reviewed by one of us or a hospital infection control practitioner using a standardized data abstraction form. Maternal demographic data, clinical information regarding treatment of maternal syphilis, and data regarding the diagnosis, evaluation, and management of the newborns were abstracted from medical records. Newborns were classified using the CDC surveillance case definitions for syphilitic stillbirths, probable syphilis cases, and confirmed cases of congenital syphilis.7,16 A syphilitic stillbirth was defined as a fetal death in which the mother had untreated or inadequately treated syphilis at delivery of a fetus after a 20-week gestation or of a fetus weighing more than 500 g. A probable case was defined as (1) an infant whose mother had untreated or inadequately treated syphilis at delivery, regardless of signs in the infant or child, or (2) an infant or child who has a reactive treponemal test result for syphilis and any 1 of the following: evidence of congenital syphilis on physical examination, any evidence of congenital syphilis on radiographs of long bones, a reactive cerebrospinal fluid (CSF) VDRL test result, an elevated CSF cell count or protein level (without cause), or a reactive fluorescent treponemal antibody absorbed 19S IgM antibody test result or IgM enzyme-linked immunosorbent assay. A confirmed case required laboratory-confirmed identification of spirochetes.7

To document local hospitals’ obstetrical screening practices for syphilis at delivery, a standardized questionnaire was used to conduct a telephone survey of obstetrical nursing supervisors at all 13 hospitals in the Minneapolis–St Paul metropolitan area where mother-infant pairs were identified. Univariate analyses were performed using standard microcomputer software to calculate rate ratios (RRs) and 95% confidence intervals (CIs).17 Differences between means of continuous variables were compared using the nonparametric Kruskal-Wallis test. P<.05 was considered statistically significant. The “capture-recapture” method outlined by McCarthy et al18 was used to estimate the completeness of case ascertainment via methods used in the study to identify probable cases of congenital syphilis and syphilitic stillbirths. The capture-recapture method uses log-linear modeling to correct for underascertainment.

RESULTS

CASE ASCERTAINMENT

Eighty-one eligible mother-infant pairs were identified from the 3 case-finding sources. One woman reported to the MDH as a syphilis case during pregnancy had a medical record that contained no evidence of syphilis, and her newborn did not have congenital syphilis; this case was excluded from the study. Sixteen newborns were identified through the MDH congenital syphilis registry, 26 newborns were identified by ICD-9 hospital discharge data, and 72 pregnant women with syphilis were identified by case reports to the MDH. Some mother-infant pairs were identified through more than one source.

MATERNAL DEMOGRAPHIC DATA

The demographic and clinical characteristics of the 80 mothers are presented in Table 1. The mothers ranged in age from 16 to 40 years; they were predominantly racial and ethnic minorities, and most were unmarried. Most mothers were insured by public assistance and resided in urban areas. Compared with demographic data on pregnant women who were delivered of newborns in the
7-county metropolitan area during the study period, the mothers in this study were significantly more likely to be minorities (RR, 4.9; 95% CI, 4.5-5.4; P < .001), to be unmarried (RR, 5.0; 95% CI, 3.3-10.0; P < .001), and to reside in an urban area (RR, 2.7, 95% CI, 2.4-3.0; P < .001). Many (44%) of these women had coexisting sexually transmitted diseases. Human immunodeficiency virus serologic test results were negative for 44 mothers (55%) and positive for 1 (1%). Human immunodeficiency virus status was unknown or not documented in the hospital birth record for 35 women (44%).

NEWBORN EVALUATION AND MANAGEMENT

Newborns were classified based on an assessment of the adequacy of maternal treatment for syphilis and clinical assessment of the newborn according to CDC guidelines. Of the 80 mother-infant pairs identified, 36 infants (45%) were classified as probable syphilis cases, 42 (53%) were noncases, and 2 (3%) were syphilitic stillbirths. None of the infants met the CDC definition of a confirmed case of congenital syphilis.

Although the mean gestational age at birth of probable cases and noncases did not differ significantly, the mean birth weight of the probable cases (2995 g) was significantly less than that of noncases (3236 g) (P = .04).

Of the 36 probable cases, 34 (94%) were asymptomatic. Thirty-one (86%) of the 36 probable cases received some clinical evaluation. Twenty (56%) of the 36 cases were evaluated adequately (ie, complete clinical examination, quantitative nontreponemal serologic tests, long bone radiographs, and CSF evaluation), 11 cases (31%) were inadequately or partially evaluated, and 5 cases (14%) were not evaluated. Twenty-six probable cases (72%) had lumbar punctures. Interpretation of CSF results was limited by missing information (10 cases) or traumatic lumbar punctures (8 cases). Table 2 summarizes the evaluation and treatment of the newborns. Two cases (6%) had clinical evidence of congenital syphilis, including 1 infant who died with severe congenital syphilis (ie, hydrops, disseminated intravascular coagulation, and neurosyphilis) hours after birth.

Twenty-five (69%) of the 36 probable cases were treated for congenital syphilis. Twenty-two (88%) of these infants were treated with 10 to 14 days of parenteral penicillin, 1 infant (4%) received 3 days of aqueous crystalline penicillin G (this infant had a normal evaluation), and 2 infants (8%) received several days of aqueous crystalline penicillin G and 1 dose of intramuscular penicillin G benzathine. Both of these 2 infants had missing CSF data.

Ten probable cases were not treated (excluding the death); only 1 of these newborns was evaluated for congenital syphilis. Eight of the 10 mothers of these newborns had inadequate or unknown treatment, 1 had received nonpenicillin therapy (erythromycin estolate), and 1 was not treated. Although the medical records indicated the physician's awareness of maternal syphilis in 9 of 10 cases, only 2 of these mothers were screened for syphilis at delivery. None of these 10 newborns had a discharge diagnosis that indicated congenital syphilis or were reported to the MDH congenital syphilis registry. Follow-up data on these newborns are unavailable.

Twenty-nine (69%) of 42 noncases had some evaluation for congenital syphilis (eg, serologic testing, long bones, radiographs, and/or CSF evaluation), and 4 noncases (10%) were treated for congenital syphilis.

MATERNAL PREGNATAL CARE AND HOSPITAL SCREENING PRACTICES

Overall, 47 women (59%) had syphilis serologic testing performed in the third trimester, and only 37 (46%) had syphilis screening at delivery. Mothers (22%) of 8 of the probable cases were first diagnosed as having syphilis at delivery. Five of the 8 mothers of probable cases diagnosed at delivery had more than 1 prenatal visit. Mothers of noncases had more prenatal visits (mean, 9) than mothers of probable cases (mean, 6) (P = .003).

Only 2 (15%) of the 13 hospitals surveyed had a protocol for syphilis screening at delivery. Of the 11 hospitals without a protocol, 9 (82%) reported that screening at delivery was performed at the discretion of the admitting physician. None of the 5 urban hospitals where most

Table 1. Characteristics of 80 Mothers Delivered of Newborns at Risk for Congenital Syphilis, Twin Cities Metropolitan Area, 1992-1994

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>n</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at delivery, mean (range), y</td>
<td>25</td>
<td>(16-40)</td>
</tr>
<tr>
<td>Race/ethnicity</td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>13</td>
<td>(16)</td>
</tr>
<tr>
<td>African American</td>
<td>48</td>
<td>(60)</td>
</tr>
<tr>
<td>Hispanic</td>
<td>6</td>
<td>(8)</td>
</tr>
<tr>
<td>Native American</td>
<td>5</td>
<td>(6)</td>
</tr>
<tr>
<td>Southeast Asian</td>
<td>4</td>
<td>(5)</td>
</tr>
<tr>
<td>Other or unknown</td>
<td>4</td>
<td>(5)</td>
</tr>
<tr>
<td>Marital status</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Not married</td>
<td>68</td>
<td>(85)</td>
</tr>
<tr>
<td>Married</td>
<td>11</td>
<td>(14)</td>
</tr>
<tr>
<td>Unknown</td>
<td>1</td>
<td>(1)</td>
</tr>
<tr>
<td>Insurance status</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Medical assistance</td>
<td>71</td>
<td>(89)</td>
</tr>
<tr>
<td>Private or health maintenance org.</td>
<td>7</td>
<td>(9)</td>
</tr>
<tr>
<td>Other</td>
<td>2</td>
<td>(3)</td>
</tr>
<tr>
<td>Residency</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Urban (Minneapolis, St Paul)</td>
<td>62</td>
<td>(78)</td>
</tr>
<tr>
<td>Suburban</td>
<td>17</td>
<td>(21)</td>
</tr>
<tr>
<td>Other</td>
<td>1</td>
<td>(1)</td>
</tr>
</tbody>
</table>

* Data are reported as number (percentage) unless otherwise indicated.

Table 2. Newborns Who Received Evaluation and Treatment for Congenital Syphilis, Twin Cities Metropolitan Area, 1992-1994

<table>
<thead>
<tr>
<th>Evaluation or Treatment</th>
<th>Probable Cases</th>
<th>Noncases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serologic testing (nontreponemal)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cord blood</td>
<td>18 (50)</td>
<td>22 (52)</td>
</tr>
<tr>
<td>Neonatal serum</td>
<td>27 (75)</td>
<td>17 (40)</td>
</tr>
<tr>
<td>Complete blood cell count</td>
<td>22 (61)</td>
<td>4 (10)</td>
</tr>
<tr>
<td>Cerebrospinal fluid</td>
<td>26 (72)</td>
<td>4 (12)</td>
</tr>
<tr>
<td>Long bone analysis</td>
<td>22 (61)</td>
<td>7 (17)</td>
</tr>
<tr>
<td>Treatment</td>
<td>25 (69)</td>
<td>4 (10)</td>
</tr>
</tbody>
</table>

*N = 80; 2 stillbirths were excluded. Data are reported as number (percentage).
(77%) of the study cases were identified had a formal policy for screening pregnant women for syphilis at delivery. However, one of these hospitals routinely performed a cord blood rapid plasma reagin test.

SENSITIVITY AND COMPLETENESS OF SURVEILLANCE METHODS

The sensitivity of each of the 3 potential congenital syphilis case ascertainment methods was calculated based on the following: (1) the assumption that all true cases of congenital syphilis were identified by at least 1 detection method and (2) the fact that all 18,332 live births occurred in the 7-county metropolitan area during the study period. The CDC surveillance case definition of a probable case of congenital syphilis or a syphilitic stillbirth was the gold standard against which sensitivity was evaluated. The MDH congenital syphilis registry identified 15 (39%) of 38 cases. The hospital discharge ICD-9 codes identified 21 cases (55%), and the MDH registry of pregnant women with syphilis identified 33 cases (87%).

All 38 cases identified cumulatively by these 3 methods were included in the reports to MDH of pregnant women with syphilis and/or the ICD-9 discharge diagnosis data; none of the 38 cases was identified solely through the MDH congenital syphilis registry. Using the capture-recapture method, the corrected number of presumptive cases of congenital syphilis and syphilitic stillbirths ascertainable using both ICD-9 discharge diagnosis data and reports to MDH of pregnant women with syphilis was estimated to be 43 (95% CI, 36-50). The percentage of these cases ascertained by the aggregate data from these 2 methods was 88% (95% CI, 76%-100%), the percentage of cases ascertained by the ICD-9 discharge data alone was 49% (95% CI, 42%-58%), and the percentage ascertained solely by data on pregnant women with syphilis was 77% (95% CI, 66%-91%).

COMMENT

Minnesota’s experience with congenital syphilis highlights several issues. First, the diagnostic evaluation and management of newborns at risk for congenital syphilis are variable and lack consistent adherence to standard protocols. The CDC’s current surveillance definition of congenital syphilis is highly sensitive and frequently may include asymptomatic infants. In addition, several published protocols vary in their definitions of a clinical case of congenital syphilis and their recommendations for evaluation of an infant at risk for congenital syphilis. These case definitions rely heavily on documentation of maternal treatment and maternal serologic status, although such data may not be readily available to the clinician. Furthermore, the interpretation of laboratory results (particularly CSF) used to evaluate these infants is hampered by poorly defined “normal” results for CSF protein and white blood cell count and the frequent occurrence of traumatic lumbar punctures.

This study demonstrates the varied approaches to the evaluation and treatment of newborns at risk for congenital syphilis. Most noncases in this study were evaluated but not treated. Other studies have reported more noncases receiving unnecessary treatment. More concerning, however, is the varied evaluation and treatment of probable cases of congenital syphilis in our study, with only slightly more than half receiving adequate evaluation, according to guidelines of the CDC and the American Academy of Pediatrics, and only two thirds of probable cases receiving treatment. Most non-treated probable cases in our study were not evaluated. It is of concern that none of these newborns was discharged with a diagnosis of congenital syphilis or reported to the MDH congenital syphilis registry, thereby limiting opportunities for follow-up of these high-risk infants.

Consistent case definitions and protocols for the evaluation and treatment of infants at risk for congenital syphilis are necessary. In 1996, Risser and Hwang proposed modifying the protocol for evaluation and treatment of asymptomatic infants born to treated mothers whose infection status is uncertain to recommend omitting the CSF and long bone analyses) and treating these infants with 1 injection of penicillin G benzathine. However, it is difficult to definitively identify these infants, and follow-up of such high-risk mothers and infants often is problematic. Glasser expressed concerns about such an approach and recommends closely adhering to the CDC guidelines for examining and treating asymptomatic newborns at risk for congenital syphilis.

Aggressive screening and follow-up of pregnant women and women of childbearing age are necessary to reduce the incidence of congenital syphilis. For populations with a high prevalence of syphilis or for high-risk patients, the CDC recommends serologic testing of pregnant women twice during the third trimester, at 28 weeks of gestation, and at delivery. Mothers affected with syphilis in this study were demographically similar (eg, urban, single, racial minorities, and insured by the public sector) to those described elsewhere in the literature. Despite these known risk factors for syphilis, fewer than half of the mothers in this study were screened for syphilis at delivery, and only 47 (59%) had serologic testing performed in the third trimester. Also, it is of concern that 22% of mothers of probable cases of congenital syphilis in this study were first diagnosed as having syphilis at delivery. At least 5 of the 8 mothers of probable cases diagnosed at delivery had more than 1 prenatal visit and thus presumably represent missed opportunities for maternal syphilis screening and treatment and the prevention of congenital syphilis.

Some states mandate screening for syphilis at delivery for all mothers; however, Minnesota does not require such screening. Although Minnesota has a low incidence of syphilis, endemic disease persists, with higher rates of early syphilis in urban areas. None of the 5 urban hospitals where most mothers in the study gave birth had a formal policy for screening pregnant women at delivery. A prior study of physicians’ practices and opinions regarding prenatal screening for sexually transmitted diseases found that of a sample of 172 family physicians and obstetricians practicing in Minnesota, only 17 (10%) routinely obtained maternal blood samples for serologic testing for syphilis at delivery. The location (ie, urban vs suburban or rural) of physicians’ clinics was not associated with their practices for syphilis screening at delivery.
Improved surveillance is needed in Minnesota to monitor and accurately describe the incidence and epidemiology of syphilis. The sensitivity of the MDH congenital syphilis registry was estimated to be only 39% in this study, suggesting that congenital syphilis may be underdiagnosed. A capture-recapture analysis of the completeness of case ascertainment in this study suggests that the case-finding methods used in the study identified 88% of the actual number of probable cases of congenital syphilis or syphilitic stillbirths; approximately 5 cases may have been undetected. The incompleteness of the surveillance data may reflect clinicians’ difficulty using congenital syphilis case definitions and/or their lack of familiarity with mandated disease reporting.

Reports to the MDH regarding pregnant women with syphilis was the most sensitive method of identifying probable cases of congenital syphilis, and perhaps expanded prenatal follow-up of these women could alert clinicians to at-risk newborns. However, this method fails to identify women first diagnosed as having syphilis at delivery. These women frequently have high-risk behaviors, such as chemical dependency, prostitution, history of incarceration, and moving from state to state.

Congenital syphilis is a public health and clinical challenge. Vigilant screening for syphilis (especially during pregnancy and delivery) is critical to eliminate congenital syphilis. Clinician adherence to standardized protocols for the evaluation and management of at-risk newborns is essential. However, revised guidelines with consistent definitions and protocols may be needed to assist physicians with this responsibility, particularly in low-incidence areas, where clinicians infrequently face this clinical challenge. Also, public health agencies responsible for disease surveillance may need new surveillance systems and additional resources to assist in the identification and follow-up of newborns at risk for congenital syphilis.

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