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Pesquisa do estreptococo do Grupo B em gestantes da Zona Leste de São Paulo
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A Study Of Group B Streptococcus In Pregnant Women Of Eastern São Paulo*

PESQUISA DO ESTREPTOCOCO DO GRUPO B EM GESTANTES DA ZONA LESTE DE SÃO PAULO

INVESTIGACIÓN DEL ESTREPTOCOCO DEL GRUPO B EN GESTANTES DE ZONA ESTE DE SÃO PAULO

Juliana Mello Função¹, Nádia Zanon Narchi²

ABSTRACT
A retrospective, cross-sectional study of 30 women seen at a Basic Health Care Unit (BHCU) in the Eastern Section of São Paulo, using interviews and medical record reviews, to determine how group B streptococcus (GBS) was detected in pregnant women. The patients in the studied sample received prenatal care at the UBS and delivered their babies between January 2009 and December 2010. Twenty-three of the women (76.7% of the total) underwent a GBS culture, 82.6% of which yielded a negative result and 17.4% of which yielded a positive result; 43.5% of these women underwent the test between 35 and 37 weeks of gestation; and 23.5% of the participants were not tested, mostly because no test was requested. GBS screening failures were shown have occurred during the selected period.

DESCRIPTORS
Streptococcus agalactiae
Streptococcal infections
Prenatal care
Mother and child health
Mother and child nursery.

RESUMO
O presente trabalho trata-se de estudo transversal e retrospectivo, realizado com trinta mulheres usuárias de uma Unidade Básica de Saúde (UBS) da Zona Leste de São Paulo, por meio de entrevista e consulta de prontuários, com o objetivo de verificar como ocorre a pesquisa do estreptococo do grupo B em gestantes. As participantes da amostra realizaram pré-natais na UBS e tiveram seus bebês no período de janeiro de 2009 a dezembro de 2010. Realizaram a cultura do EGB 23 mulheres (76,7% do total), 82,6% com resultados negativos e 17,4%, positivos; 43,5% delas realizaram o exame entre 35 e 37 semanas de gestação; 23,5% não realizaram o exame, a maior parte por ausência de solicitação. Foi possível verificar que ocorreram falhas no rastreamento do EGB durante o período selecionado.

DESCRIPTORES
Streptococcus agalactiae
Infecciones estreptocócicas
Cuidado pré-natal
Saúde materno-infantil
Enfermagem materno-infantil

RESUMEN
Estudio transversal y retrospectivo, realizado con 30 mujeres pacientes de una Unidad Básica de Salud (UBS) de la Zona Este de São Paulo mediante entrevista y consulta de historias clínicas, con el objetivo de verificar como se efectúa la investigación de estreptococos del grupo B en gestantes. La muestra realizó prenatal en la UBS y tuvo sus bebés en el período de enero de 2009 a diciembre de 2010. Veintitrés mujeres (76.7% del total) realizaron la cultura de EGB, 82,6% con resultados negativos y 17,4% positivos; 43,5% de las pacientes realizaron el examen entre las semanas 35 y 37 de gestación; 23,5% no realizaron el examen, la mayor parte por no haber efectuado la solicitud. Fue posible verificar que ocurrieron fallas en el rastreo del EGB durante el período seleccionado.
INTRODUCTION

Group B streptococcus (GBS) or Streptococcus agalac-tiae is a bacterium commonly found in women. GBS colo-nizes the genital tract, originating from its main reservoir, the gastrointestinal tract and, less frequently, from the urinary tract. It is estimated that 15 to 40% of pregnant women have GBS in the vagina and/or rectum and that approximately 50 to 75% of newborns exposed to GBS become colonized before or after delivery; however, this colonization does not necessarily lead to the development of a neonatal infection or disease.

During the pregnancy-puerperal cycle, GBS may cause urinary infections, endometritis, chorioamnionitis, postpartum wound infections and puerperal sepsis. Furthermore, the bacterium may jeopardize the progress of the gestation, causing abortion, intrauterine fetal death, premature rupture of membranes and preterm delivery.

During the neonatal period, the infection manifests clinically in two forms. Early-onset disease occurs in two-thirds of cases and appears during the first 24 hours of life. It is characterized by sepsis, respiratory distress, apnea, pneumonia and meningitis. In comparison, late-onset disease manifests between seven and 90 days after delivery (the mean onset time is 27 days); in half of all cases, it is associated with nosocomial infection, and its main result is meningitis.

The first maternal-fetal infection prophylaxis strategy that was internationally proposed and adopted was developed in 1996 by the Centers for Disease Control and Prevention (CDC) and the American College of Obstetricians and Gynecologists (ACOG). It recommended searching for the following GBS risk factors: labor before completing 37 weeks of gestation, even in the presence of an intact amniotic sac; term labor lasting longer than 18 hours with a ragged amniotic sac; unexplainable fever during labor; neonatal GBS infection during a previous pregnancy; and present or past GBS infection of the urinary tract.

In 2002, the CDC decided to exclude this risk search because half of the cases of early sepsis in newborns did not have any of the abovementioned risk factors. Another argument supporting the change in criteria was the unnecessary use of antibiotics in women who were not colonized by GBS. For those reasons, the CDC’s recommended prophylactic strategy was changed to recommend the prenatal screening of GBS in material collected from the vaginal entrance and perianal region of all pregnant women during the 35th to 37th week of pregnancy.

Cultures collected earlier are unable to predict whether the woman will be colonized at delivery, given that samples collected four weeks before labor can identify maternal colonization at birth with greater sensitivity and specificity, and sample collection must be repeated if delivery does not occur within that period.

According to the technical note of the Mâe Paulistana Project, which follows the recommendations of the CDC and of the Ministry of Health (MS), the Basic Health Care Service should track GBS; that is, all pregnant women must undergo vaginal and rectal secretion culture between the 35th and 37th week of pregnancy.

Variations in the prevalence of GBS colonization in pregnant women are related to differences in both women’s characteristics, such as age, parity, socioeconomic level and geographic location, and the culture methods used. Studies conducted at hospitals in the Brazilian states of Paraná, Santa Catarina, São Paulo and Maranhão showed prevalences of 14.9%, 21.6%, 14.6% and 20.4% for GBS, respectively.

Although tracking is accessible and sample collection is simple, GBS cultures are not currently routinely conducted during prenatal care. Scarce information about the occurrence of the infection may be partially responsible for the insufficient attention provided by relevant institutions, in terms of both prenatal screening and proper prophylaxis during the labor of colonized women. These reasons justify the conduct of this trial.

The purpose of this study was to determine how GBS is investigated in pregnant women assisted during prenatal care in a Basic Health Care Unit (UBS) in the eastern section of São Paulo.

METHODS

This is a retrospective, descriptive and cross-sectional study with a quantitative approach. It was conducted at UBS “Cidade Pedro José Nunes”, located in the district of São Miguel in the eastern section of São Paulo. This UBS serves an estimated population of 20,000 people and includes five Family Health Care Strategy (ESF) teams.

The Basic Health Care Information System (SIAB) indicated that a total of 208 women in the UBS had babies born between January 2009 to December 2010. Based on that information, the 208 medical records were recorded in a table and individually analyzed.

The Community Health Care Agents (ACS) indicated that only 104 subjects had completed their prenatal care follow-up and continued to live in the UBS coverage area. Their medical records were numbered and, using a simple lottery without replacement, we composed a probabilistic sample of simple random type for 25% of the population. The sample selected was 26 subjects, one for every five.
the population; that is, 30 women. Those women were subsequently contacted by the Community Health Care Agents to check their availability to be visited at home. Because there were no refusals, data collection interviews were scheduled.

The inclusion criteria used to compose the sample were women who matched the profile search; that is, those who had had prenatal care follow-up at the UBS, had delivered between January 2009 and December 2010 and had agreed to participate in the study. The exclusion criteria were women who refused to participate or who had moved from the coverage area.

The initial data collection was based on the 30 medical records. Data related to the pregnancy-puerperal period and to GBS collection were verified. Next, the participants were personally interviewed to collect additional data relating to pregnancy, labor and puerperium, newborn conditions and whether samples were taken to detect GBS.

The following variables were used to verify how GBS was detected: gestational age (GA) on the date of the examination collection; explanations about the procedure, importance and result; a prenatal card with an annotation of the culture result; guidance received in response to a positive culture; and reasons presented for not conducting the examination.

Regarding gestational age, it is important to note that it was corrected when the data were collected in the medical records to estimate the gestational age at which the examination was actually taken, based on the earliest obstetric ultrasound (USG), that is, the one conducted during the first gestational quarter.

At the time of the home visit and before the interview, all participants were duly informed about the study’s purposes and relevance and about the maintenance of confidentiality, personal anonymity and the free right to participate, as determined by Resolution 196/96 and in accordance with the Instrument of Free Informed Consent. The data were collected after approval from the Research Ethics Committee of the Health Care Office of São Paulo (CEP/SMS), Opinion Nº 402/10, and proper authorization of the people in charge of the Health Care Supervision and the UBS.

All data were analyzed in a descriptive manner. The statistical package used was Epi-Info 3.5.2. from the World Health Organization (WHO).

**RESULTS**

Sociodemographically, the sample was composed of self-declared Caucasian women (66.7%) with an age equal to or older than 20 years (76.7%), nine or more years of education (70%) and a family income of one to two minimum salaries (70%) who were living with a partner in a stable relationship (40%) and were nonsmokers (93.3%).

A culture for GBS detection was taken in 76.7% of the women, of whom 82.6% had a negative result and 17.4% had a positive result. This indicated an accurate GBS prevalence of 17.4%.

Table 1 displays the sociodemographic characterization of the sample in accordance with the GBS culture performance and results.

**Table 1** - Sociodemographic characterization in accordance with GBS – São Paulo, 2011

<table>
<thead>
<tr>
<th>Variables</th>
<th>GBS positive</th>
<th>GBS negative</th>
<th>No GBS</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
<td>%</td>
<td>N</td>
</tr>
<tr>
<td>Self-declared race or skin color</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Caucasian</td>
<td>3</td>
<td>10.0</td>
<td>13</td>
</tr>
<tr>
<td>Non-Caucasian</td>
<td>1</td>
<td>3.3</td>
<td>6</td>
</tr>
<tr>
<td>Age (years)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 20</td>
<td>-</td>
<td>-</td>
<td>5</td>
</tr>
<tr>
<td>&gt; or = 20</td>
<td>4</td>
<td>13.3</td>
<td>14</td>
</tr>
<tr>
<td>Education</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 to 8 years of education</td>
<td>2</td>
<td>6.7</td>
<td>6</td>
</tr>
<tr>
<td>9 or more years of education</td>
<td>2</td>
<td>6.7</td>
<td>13</td>
</tr>
<tr>
<td>Family income</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Up to 1 MS*</td>
<td>1</td>
<td>3.3</td>
<td>2</td>
</tr>
<tr>
<td>1 to 2 MS</td>
<td>3</td>
<td>10.0</td>
<td>13</td>
</tr>
<tr>
<td>More than 2 MS</td>
<td>-</td>
<td>-</td>
<td>4</td>
</tr>
</tbody>
</table>
Regarding the gynecological-obstetric characterization, the sample was mostly composed of multiparous women (70%) with no previous abortion (86.7%), no report of sexually transmitted disease (93.3%) and with a report of urinary infection during or before the last pregnancy (53.3%). The women reported that during the last delivery, they had delivered their babies vaginally (70%), with a gestational age higher than or equal to 37 weeks (93.3%), no premature rupture of membranes (86.7%) and no fever during or after labor (96.7%).

Table 2 shows the women's gynecologic and obstetric components in accordance with the GBS culture performance and results.

<table>
<thead>
<tr>
<th>Variables</th>
<th>GBS positive</th>
<th>GBS negative</th>
<th>No GBS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Marital status</td>
<td>N %</td>
<td>N %</td>
<td>N %</td>
</tr>
<tr>
<td>Single</td>
<td>- -</td>
<td>6 20.0</td>
<td>1 3.3</td>
</tr>
<tr>
<td>Married</td>
<td>3 10.0</td>
<td>8 26.7</td>
<td>- -</td>
</tr>
<tr>
<td>Stable relationship</td>
<td>1 3.3</td>
<td>5 16.7</td>
<td>6 20.0</td>
</tr>
<tr>
<td>Smoker</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>- -</td>
<td>2 6.7</td>
<td>- -</td>
</tr>
<tr>
<td>No</td>
<td>4 13.3</td>
<td>17 56.7</td>
<td>7 23.3</td>
</tr>
</tbody>
</table>

* MS: minimum salary.

Table 2 - Gynecologic-obstetric characterization in accordance with GBS – São Paulo, 2011

<table>
<thead>
<tr>
<th>Variables</th>
<th>GBS positive</th>
<th>GBS negative</th>
<th>No GBS</th>
</tr>
</thead>
<tbody>
<tr>
<td>N %</td>
<td>N %</td>
<td>N %</td>
<td>N %</td>
</tr>
<tr>
<td>Number of pregnancies</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>One</td>
<td>- -</td>
<td>7 23.3</td>
<td>2 6.7</td>
</tr>
<tr>
<td>Two</td>
<td>1 3.3</td>
<td>9 30.0</td>
<td>2 6.7</td>
</tr>
<tr>
<td>Three</td>
<td>2 6.7</td>
<td>1 3.3</td>
<td>- -</td>
</tr>
<tr>
<td>Four</td>
<td>1 3.3</td>
<td>2 6.7</td>
<td>2 6.7</td>
</tr>
<tr>
<td>Five or more</td>
<td>- -</td>
<td>- -</td>
<td>1 3.3</td>
</tr>
<tr>
<td>Parity</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Primiparous</td>
<td>- -</td>
<td>7 23.3</td>
<td>2 6.7</td>
</tr>
<tr>
<td>Multiparous</td>
<td>4 13.3</td>
<td>12 40.0</td>
<td>5 16.7</td>
</tr>
<tr>
<td>Previous abortion</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>1 3.3</td>
<td>1 3.3</td>
<td>2 6.7</td>
</tr>
<tr>
<td>No</td>
<td>3 10.0</td>
<td>18 60.0</td>
<td>5 16.7</td>
</tr>
<tr>
<td>STD report</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>- -</td>
<td>2 6.7</td>
<td>- -</td>
</tr>
<tr>
<td>No</td>
<td>4 13.3</td>
<td>17 56.7</td>
<td>7 23.3</td>
</tr>
<tr>
<td>Gestational age at the last delivery</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 37 weeks</td>
<td>- -</td>
<td>2 6.7</td>
<td>- -</td>
</tr>
<tr>
<td>≥ 37 weeks</td>
<td>4 13.3</td>
<td>17 56.7</td>
<td>7 23.3</td>
</tr>
<tr>
<td>Premature rupture of membranes in the last delivery</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>1 3.3</td>
<td>2 6.7</td>
<td>1 3.3</td>
</tr>
<tr>
<td>No</td>
<td>3 10.0</td>
<td>17 56.7</td>
<td>6 20.0</td>
</tr>
<tr>
<td>Duration of ruptured membranes in the last delivery</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 18 hours</td>
<td>3 10.0</td>
<td>18 60.0</td>
<td>6 20.0</td>
</tr>
<tr>
<td>≥ 18 hours</td>
<td>1 3.4</td>
<td>1 3.3</td>
<td>1 3.3</td>
</tr>
<tr>
<td>Urinary infection during or before the last pregnancy</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>2 6.7</td>
<td>10 33.3</td>
<td>4 13.3</td>
</tr>
<tr>
<td>No</td>
<td>2 6.7</td>
<td>9 30.0</td>
<td>3 10.0</td>
</tr>
</tbody>
</table>
Regarding the GBS search, 73.9% of the women reported that they were informed about how the collection procedure was performed and its importance, and 87% were informed about the culture result before labor. Only 78.3% of the prenatal cards included information about the culture collection and result: the gestational age on the date of examination collection was less than 35 weeks in 52.2% of the instances, 35 to 37 weeks in 43.5% cases and greater than 37 weeks in 4.3% of cases.

Among the women whose culture result was positive (17.4%), all of them stated that they were instructed during the prenatal care follow-up about the meaning of a positive finding and the need for prophylaxis with antibiotics at delivery. Nevertheless, a user with a positive culture reported that she did not receive any type of antibiotics during the labor and delivery process.

In the cases in which no culture was performed (23.3%), the reason reported by most of the subjects (85.7%) was that the professional assisting them during the prenatal care follow-up did not request a culture. All of the subjects stated that they would have undergone the examination if it had been requested, especially because of its importance and the possible consequences of the infection to the newborn.

**DISCUSSION**

Few studies in Brazil demonstrate the prevalence of maternal and neonatal GBS colonization, and the universal search protocol for pregnant women is also recent in the State of São Paulo.

Studies show that it is not possible to select a group of women with high probability of being colonized by GBS upon labor, despite the risk factors that have been identified in the literature. Research shows that pregnant women with any of the aforementioned risk factors, but with a negative GBS culture, were considered at low risk for early neonatal infection, with an incidence of 0.9 cases/1000 births. In women with a positive culture and no risk factor, the incidence is 5.1 cases/1000 births.

A study conducted by the CDC concluded that the tracking strategy, in which cultures are collected from all pregnant women between 35 and 37 weeks, is 50% more effective for preventing early GBS infection than the strategy based on risk factors is. However, the maximum efficiency of the tracking procedure depends on certain factors, such as the collection site, which is mandatorily vaginal and anal-retal, the quality of the material collected, the bacteriologic technique used and the gestational age.

This study only focused on the gestational age factor and did not evaluate the collection sites, the type of material collected or the microbiological methods used. For that purpose, it is important to emphasize that the UBS from which the patients in this study were selected follows the GBS tracking recommendations described in the technical note of the Mãe Paulistana Project.

However, the results of this study show that in only 43.5% of the women, material was collected at the prescribed gestational age. In most instances, the examinations were conducted outside the period recommended by the CDC. It should be emphasized again that this period is indicated because of the increased sensitivity and specificity of cultures made within four weeks before labor.

One of the possible reasons that not all of the samples were collected during the recommended period may be errors in estimating gestational age, which is often based on an inaccurate last menstruation date (LMD) or, more frequently, on USG conducted during the second or third gestational trimester, both of which have significantly greater error estimates. In that regard, it is important to note that the obstetric USG is the most effective method for pregnancy dating, especially when it is conducted in the first trimester of pregnancy. It should be noted that
the lack of accuracy in the gestational age as estimated by
the last menstruation date results mainly from the subjects
inaccurate memory of the event and the occurrence of
irregular menstrual cycles.

The inadequacy of gestational age at the examination col-
lection may also be related to the health care professionals
unfamiliarity with or improper interpretation of the protocol.
Consequently, the health care professional may consider it
more important to perform the examination at any given time
during the pregnancy and at his/her discretion.

The correct determination of the gestational age is
fundamental for the proper pregnancy follow-up and re-
ducing unnecessary interventions. Its accurate definition
is highly important in extreme cases of fetal viability, in
terms of both premature births and prolonged pregnan-
cies. Thus, the gestational age estimate between the
11th and 14th week of pregnancy, which is determined
by measuring the cranial-caudal fetal length, features a
maximum error of one week(16). On the other hand, when
such estimates are made near the 20th or 30th gestational
week, the error changes to one and a half weeks and two
and a half weeks, respectively.

When comparing the LMD with the obstetric USG car-
ried out early, studies(16-17) show that estimates based on the
last menstruation date tend to overestimate the gesta-
tional age, especially at gestational extremes, thus increasing
the ratio of postterm pregnancies and underestimating premature labors. As a result, the last menstruation date
may differ from the ultrasound estimate by approximately
two to 14 days.

In this study, the overestimation of gestational age
may be related to the small number of requests for GBS
culture for women more than 37 gestational weeks into
their pregnancies (4.3% of the cases) or to the high number
of cultures made before the proper period (52.2% of the
cases). Furthermore, the cases for which no examinations
were requested (23.3%) may be related to the health care professional’s lack of knowledge about the protocol
or the proper method of pregnancy dating, as previously
discussed.

Among the interviewed women who underwent a cultu-
re, most were informed about the examination’s purposes,
its importance and the consequences of the infection for
the newborn. Many multiparous women even asked why
the culture was not performed during their previous preg-
nancies. It should be noted that 26.1% of the women stated
that they were not instructed about the procedure or the
importance of the examination. They were only told that
it should be performed.

An interesting fact worth highlighting is the contact
established between the users and the Community Health
Care agents who contributed to the progress of the study. All
of these individuals made themselves available to schedule
the home visits, stated that they knew precisely which users
had undergone the examination and, most importantly,
which ones had had a positive culture result.

In that regard, it should be noted that the ESF(18) began
in the middle of 1993 as a program of the Brazilian Ministry
of Health to change the traditional manner of providing
health care, with the aim of promoting health and providing
full assistance to the user as a subject integrated into the
family, the home and the community. Among other aspects,
this purpose requires linking professionals and services to
the community and positions the Community Health Care
agents as the link between the population, the professionals
and the health care service.

Among the women whose GBS culture was positive, only
one reported that she did not receive intralabor antibiotic
prophylaxis, which should begin four hours before the birth.
The efficacy of this treatment is approximately 25 to 30%,
and it may reduce newborn mortality in 10% of cases(19). The
only indication for starting treatment during pregnancy is
urinary infection caused by GBS.

This woman reported that she was told that she
could not receive the antibiotics because she was having
a surgical delivery for a reason unknown to her. In such
instances, the literature(12) indicates that prophylaxis is
unnecessary only in cases of elective cesarean section,
given that the risk for neonatal disease is low. However,
when antibiotics are used during a surgical delivery, they
should be administered when the surgical incision is made
rather than four hours before the birth, as recommended
for vaginal delivery.

Several risk factors for neonatal GBS infection have
already been identified. The most important of these is
maternal colonization, which increases the risk to the
newborn by approximately 200 times(19). Neonatal infection
rates greater than 0.6/1000 live births (NV) indicate the
need to establish prophylaxis by identifying maternal risk
factors, while rates greater than 1.2/1000 NV require the
universal culturing during prenatal care, with a favorable
cost-effectiveness relationship.

These rates have only recently been determined in Bra-
zil. A study conducted in Campinas(19) showed a neonatal
GBS infection incidence of 1.4/1000 NV, thus confirming
the need for universal tracking in pregnant women. Furthe-
more, in accordance with the CDC(12), the introduction of
a structured prophylaxis scheme reduces the incidence
of streptococcal disease of early onset in newborns in almost
70%, from 1.5 to 0.5 per 1000 NV.

CONCLUSION

Irrespective of the study limitations related to the screen-
ing bias, the reduced sample size and the impossibility
of a more complex statistical analysis, it was possible to
conclude that failures in GBS tracking occurred during the
period determined for this study.
Only 76.7% of the women were cultured for GBS, resulting in 82.6% negative results and 17.4% positive results. Only 43.5% of the cultures were collected between 35 and 37 gestational weeks. Of the 23.3% of the women who did not undergo the examination, most reported that it was because their health care provider did not request an examination.

It was also possible to verify that errors occurred in the gestational age estimates of women who did not undergo GBS screening and those whose culture samples were collected before or after the recommended period. For that purpose, it is important to note that all of the medical records that were consulted included discrepancies in the reported gestational ages, some of which were based on the last menstruation date and others on obstetric USG. These discrepancies interfering with the pregnancy dating and determining the proper time to perform the examination.

Because it is impossible to select a group of women with high probability of being colonized by GBS during labor, the universal tracking of all pregnant women during the prenatal care follow-up is critical. Universal screening can identify a larger number of colonized pregnant women and thereby decrease the incidence of neonatal infection, which unfortunately did not occur among all the women who were randomly selected for screening in this study.

REFERENCES


