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# Number of colony forming units in urine at 35–37 weeks' gestation as predictor of the vaginal load of Group B *Streptococci* at birth

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ABSTRACT

*Objective:* To evaluate GBS colony numbers in the urine at 35–37 weeks' gestation to predict the load of GBS-colonization of the vagina at birth.
*Study design:* In this prospective observational study, we included 902 unselected pregnant women. Exposure was GBS colony forming units (CFU) per mL urine at 35–37 weeks' gestation. Outcome was vaginal GBS colonization at birth as assessed by a semi-quantitative culture of a vaginal swab sample (negative, +1, +2, +3).
*Results:* Bacteriuria with GBS at 35–37 weeks' gestation performed with a sensitivity of 30% concerning any degree of vaginal GBS colonization at birth (31 of 104 cases); 19% for light (+1), 17% for medium (+2), and 52% for high load (+3) vaginal GBS colonization. The colony count in case of GBS bacteriuria at 35–37 weeks' gestation performed with positive predictive values of 35% for $<10^4$ CFU/mL, 70% for $10^4$ CFU/mL, and 67% for $>10^4$ CFU/mL.
*Conclusion:* Even though the urinary GBS CFU at 35–37 weeks' gestation is strongly associated with a high load of vaginal GBS colonization intrapartum, it may not perform satisfactorily as a standalone-screening marker for risk of early-onset GBS disease.



## Introduction

Bacteriuria with Group B *Streptococci* (GBS) during pregnancy may constitute a marker for a high load of genital tract colonization with GBS, and it constitutes a risk factor for early-onset GBS disease (EOGBS) [1–3]. Therefore, identification of GBS in urine might be a useful screening tool for identification of women at risk of transferring GBS to their infant at birth.

We know only little about the association between the antepartum GBS-urinary colony count and the load of GBS in the vagina intrapartum. If this association is strong, quantification of GBS in the urine may constitute an effective tool for assessing the risk of EOGBS and minimizing the number of women who should be screened for vaginal GBS colonization intrapartum by a polymerase chain reaction (PCR) test. If the quantitative association is very strong, the antepartum GBS screening of urine might even replace the intrapartum vaginal PCR-GBS test, which is usually not quantitative [4,5] and is perhaps too sensitive, thus finding small and clinical insignificant numbers of GBS in the vagina.

The aims of this study were to assess the performance of screening for GBS in urine at 35–37 weeks' gestation to identify women with vaginal GBS colonization during labor, and furthermore, to evaluate whether the urinary GBS colony-count provides further information regarding the load of GBS in the vagina.

## Material and methods

### Study design

In this prospective observational study, we included 902 pregnant women at a gestational age of 29 weeks [4]. Detailed information on oral antibiotic use during pregnancy was obtained from the registered data in medical records and delivered from the

*Abbreviations:* CI, confidence interval; CFU/mL, colony-forming units per mL; EOGBS, early onset of neonatal group B streptococcal disease; GBS, Group B *Streptococci*; $GBS_{urine35-37\ weeks}$, GBS in urine at 35–37 weeks' gestation; $GBS_{vaginabirth}$, GBS in vagina at labor; $GBS_{vagina35-37weeks}$, GBS in vagina at 35–37 weeks' gestation; IAP, intrapartum antibiotic prophylaxis; NPV, negative predictive value; PCR, polymerase chain reaction; PPV, positive predictive value.

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Danish Medical Agency's Register of non-hospitalized patient use, which included records on all drug prescriptions filed at any Danish pharmacy [6].

*Inclusion criteria*

- Pregnant women attending the prenatal Clinic at Lillebaelt Hospital, Kolding, Denmark. All pregnant women in the catchment area of Lillebaelt Hospital give birth at this clinic, as there are no private or other public alternatives. Only very complicated pregnancies like extreme preterm births are referred to University Hospitals.

*Exclusion criteria*

- Women treated with antibiotics after 35 weeks' gestation.
- Preterm labor (before $37^{+0}$ weeks gestation).
- Age under 18 years.
- Women with a communication barrier such as language or mental health conditions.

*Collection and culture of specimens*

At 35–37 weeks' gestation, each participant delivered a Clean Catch Midstream urine specimen for conventional quantitative culture during the planned visit to the midwife outpatient clinic. Urine samples were seeded on a 5% blood agar plate at Department of Clinical Microbiology, Vejle Hospital, Denmark and read after incubation at 35 °C for 24 or 48 h depending on the initial growth of bacteria. GBS was identified as described below and the bacteriuria classified according to the number of colony-forming units per mL (CFU/mL). Low colony counts refer to $<10^4$ CFU/mL, and high colony counts refer to $\geq 10^4$ CFU/mL.

A vaginal ESwab sample was obtained from each participant by self-administered sample collection at 35–37 weeks' gestation and during labor by the midwife. Samples were cultured for GBS at the time of arrival to the laboratory; if received after 8 PM, they were kept at 4 °C until the next morning. Direct plating without prior enrichment of the specimen in a culture broth was carried out by streaking the ESwab specimen on a selective Granada agar plate. The vaginal swabs from the same patient were seeded on split sides of the same Granada agar plate (BioMérieux®, Spain). The Granada agar plates were incubated immediately after the seeding in a 35 °C in $CO_2$-containing atmosphere. All samples were analyzed at the Department of Clinical Microbiology, Lillebaelt Hospital, Vejle, Denmark. All GBS-like colonies (identified by their orange color on Granada agar plates) were routinely confirmed as *Streptococcus agalactiae* using the Microflex LT ™ MALDI-TOF system (Bruker Daltonik, Germany). Growth was classified semi-quantitatively as plates having only growth of a few GBS colonies (1 + ), some (2 + ) or many (3 + ). Twenty-seven culture tests were mistakenly not recorded with a semi-quantitative assessment result: 21 were urine culture negative at 35–37 weeks' gestation, 6 were urine culture positive, of which 2 had a colony count $<10^4$ CFU/mL and 4 had a colony count = $10^4$ CFU/mL.

*Ethics*

The study was approved by the Regional Scientific Ethical Committees for Southern Denmark (S-20130089) and the Danish Data Protection Agency (2008-58-0035). All participants provided written informed consent.

*Statistics*

STATA Statistics/Data Analysis software (version 14; StataCorp LP) was used for the statistical analysis. The results of the categorical variables were expressed as percentages, with a 95% corresponding confidence interval (CI). Differences in proportions were compared using either the chi-square test or Fisher's exact test. P values below 0.05 were considered statistically significant. Odds ratios are used to assess associations. Sensitivity, specificity, positive predictive value (PPV) and negative predicative value (NPV) of both antenatal vaginal cultures and urine cultures were calculated to evaluate their accuracy in predicting GBS colonization at the time of delivery.

## Results

Within the population of 902 unselected pregnant women, the rate of GBS-uria at 35–37 weeks' gestation ($GBS_{urine35-37weeks}$) was 5.9% (53/902), whereas the rate of GBS in vagina at birth

**Table 1**
Demographic characteristics of the participants.

| Number of participants = 902 | $GBS_{urine\ 35-37\ weeks}$ | | | | | | |
|---|---|---|---|---|---|---|---|
| | Positive (N = 53) | | Negative(N = 849) | | OR | 95% CI | P-value |
| Maternal characteristics | Number | % | Number | % | | | |
| **Age of the mother** | | | | | | | |
| Under 25 | 3 | 5.7 | 84 | 9.9 | 0.55 | 0.17–1.79 | 0.32 |
| 25–34 | 41 | 77.4 | 573 | 67.5 | 1.65 | 0.85–3.18 | 0.14 |
| 35 and above | 9 | 17 | 192 | 22.6 | 0.7 | 0.34–1.46 | 0.34 |
| **Parity** | | | | | | | |
| 1 | 22 | 41.5 | 385 | 45.4 | 0.81 | 0.49–1.50 | 0.54 |
| 2 | 26 | 49.1 | 420 | 49.5 | 0.99 | 0.57–1.73 | 0.95 |
| 3 or more | 5 | 9.4 | 44 | 5.2 | 1.91 | 0.72–5.03 | 0.19 |
| **Body mass index** | | | | | | | |
| Under 24.9 | 33 | 62.3 | 544 | 64.1 | 0.93 | 0.52–1.64 | 0.79 |
| 25–29.9 | 13 | 24.5 | 194 | 22.9 | 1.1 | 0.58–2.09 | 0.78 |
| 30- or more | 7 | 13.2 | 111 | 13.1 | 1.01 | 0.45–2.30 | 0.98 |
| **Tobacco** | | | | | | | |
| Never smoking | 48 | 90.6 | 779 | 91.8 | 0.86 | 0.33–2.24 | 0.76 |
| Stopped in pregnancy | 3 | 5.7 | 24 | 2.8 | 2.06 | 0.60–7.08 | 0.25 |
| Smoke ≤ 10 cigarettes | 1 | 1.9 | 34 | 4 | 0.46 | 0.06–3.43 | 0.45 |
| Smoke > 10 cigarettes | 1 | 1.9 | 12 | 1.4 | 1.34 | 0.17–10.5 | 0.78 |