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Maternal Group B Streptococcus Infection Correlates Inversely With Preeclampsia in Pregnant African American Women

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Abstract

Objective: To determine whether an association exists between group B Streptococcus (GBS) colonization and preeclampsia among pregnant Black women.

Methods: This retrospective cross-sectional study involved Black women who gave birth at State University of New York Downstate Hospital between January 2010 and December 2017. Data were collected from the Obstetric Department, including delivery date, time, mode of delivery, age of the mother, weeks of gestation at delivery, and antepartum complications. The GBS test results were originally determined using the eSwab transport system. Preeclampsia was defined based on the American College of Obstetricians and Gynecologists criteria for the periods 2010–2012 and 2013–2017. The primary outcome was whether GBS was associated with the outcome of preeclampsia in the population of Black women. Covariates, including smoking status, gestational age, parity, body mass index, maternal age, and presence of herpes simplex virus (HSV) and human immunodeficiency virus (HIV) were examined as potential confounders. Chi-squared test and logistic regression model were used, presenting odds ratios with 95% confidence intervals ($P < 0.050$), analyzed with SAS on Demand for Academics (SAS Institute, Inc., NY).

Results: Among the 8,019 Black women included in this study, GBS-positive women ($n = 977$) had a 53% reduction in the likelihood of being diagnosed with preeclampsia compared to GBS-negative women (adjusted odds ratio, 0.47; 95% confidence interval, 0.32–0.70). We did not find evidence of differences in the distribution of smoking habits ($P = 0.783$) or maternal age ($P = 0.107$) between GBS-positive and GBS-negative women. However, the GBS-positive women tended to be less likely to have a preterm delivery (9.62% (94/977) *vs.* 24.24% (1707/7042), $P < 0.001$), less likely to be nulliparous (33.37% (326/977) *vs.* 37.87% (2667/7042), $P = 0.006$), and less likely to be obese (51.38% (502/977) *vs.* 55.30% (3894/7042), $P < 0.001$) compared with GBS-negative women. In contrast, GBS-positive women were more likely to have a comorbid infection than their counterparts: HSV (5.94% (58/977) *vs.* 2.63% (185/7042), $P < 0.001$) and HIV (1.54% (15/977) *vs.* 0.82% (58/7042), $P = 0.028$).

Conclusion: We found a reduced likelihood of preeclampsia among women who were positive for GBS at delivery. Given the cross-sectional nature of our study, more research is needed to further explore this association.

Keywords: Pregnancy outcome; Preeclampsia; GBS colonization; African American; Afro-Caribbean

Introduction

Group B streptococcus (GBS) is a β-hemolytic, gram-positive bacterium that asymptomatically colonizes the lower genital tract (cervix, vagina, and vulva) of approximately 18% of women worldwide.[1,2] Globally, the prevalence of maternal GBS colonization is highest in Africa (~22%) and lowest in Asia (~11%).[3,4] In the United States, the estimated prevalence of maternal GBS colonization is approximately 19%.[3] During pregnancy, however, if GBS ascends from the vagina to the intrauterine space, it becomes highly pathogenic and is associated with numerous maternal and fetal complications such as preterm birth, stillbirth, and neonatal infections.[1,2] In particular, GBS remains a leading cause of sepsis and meningitis in infants in the first 90 days of life.[5] Since antepartum infections trigger a maternal immune response and change the inflammation phenotype,[6] it is speculated that maternal GBS colonization may also change the inflammation associated with preeclampsia thus affecting the preeclampsia development.

Reports examining whether GBS colonization in pregnant women affects the incidence of preeclampsia have yielded inconclusive results. In a cross-sectional study using two statewide hospital databases (Florida, 2001: 190,645 pregnant women;

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Texas, 2004–2005: 577,153 pregnant women), the presence of GBS was inversely associated with preeclampsia.[7] However, in a case-control study of 330 pregnant women at a hospital in Texas in 2010–2012, there was no association of GBS with preeclampsia.[8] More recently, a single center, retrospective cohort study of 60,029 births at Duke Health affiliated hospitals in North Carolina, during 2003–2015, also found that GBS colonization was not associated with preeclampsia.[9]

The reasons for these discrepancies are not immediately apparent, but factors such as race and ethnicity may contribute. Preeclampsia is more prevalent in Black women than in women of other races.[10,11] Group B Streptococcus colonization also varies among races, with Black women having the highest prevalence.[3,12–16] In the cited studies, the proportion of Black patients ranged from 1.5%–35%. We hypothesized that if a predominantly Black population were studied, the hypothesized higher prevalence of GBS and preeclampsia would allow greater statistical power in detecting whether a relationship exists between the two. The purpose of the current study is to test this hypothesis using data from the predominantly Black population of our hospital.[17] To carry out this goal, we analyzed patient records from January 2010 to December 2017.

Methods

This retrospective cross-sectional study enrolled 11,770 women who delivered between January 2010 and December 2017 at the University Hospital at SUNY Downstate, limited to 8,019 Black women after specific exclusions and accounting for missing participants. This hospital primarily serves a Black population composed of Afro-Caribbean and African immigrants as well as African Americans.[17] We excluded women diagnosed with chronic hypertension, gestational diabetes, and type II diabetes to remove the confounding effect of these comorbid conditions. We also excluded women with a gestational age delivery before 20 weeks. Thus, a total of 1,413 were excluded. Women missing information on GBS status, maternal age, race, and body mass index (BMI) were also excluded from the population (n = 2,338) (Fig. 1).

Data from hard copies of delivery records in the obstetric department, along with electronic medical records when available accounting for the record of every birth, were evaluated. Information including the date, time, mode of delivery, age of the mother, weeks of gestation at delivery, and antepartum complications, along with corresponding clinical details for each patient, was compiled into a Microsoft Excel database.

Exposure

A GBS swab was performed using the eSwab transport system (COPAN Italia, Brescia, Italy) to swab the vagina and rectum, as per the methods employed during the original data collection process. The samples were subsequently transported to the clinical pathology laboratory of SUNY Downstate University Hospital for GBS culture. The diagnosis and GBS's sensitivity to penicillin were made by an experienced clinical pathologist at SUNY Downstate University Hospital.

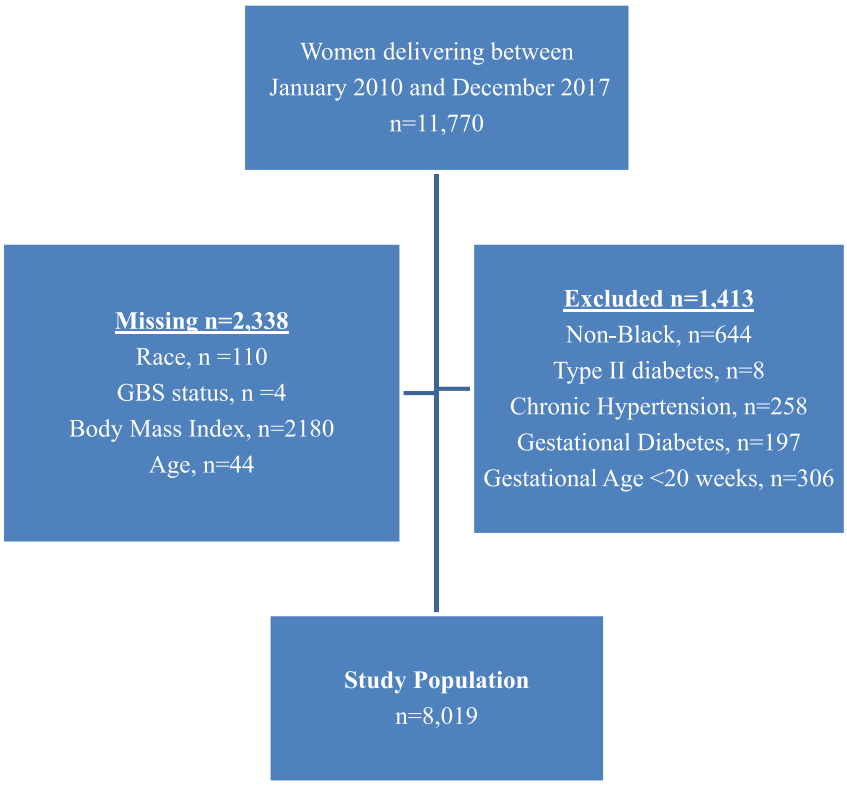

Figure 1. Flowchart showing the inclusion and exclusion criteria used to obtain the final study population. GBS: group B Streptococcus.

Outcome

The primary outcome of the study is whether GBS is associated with the outcome of preeclampsia in the population of Black women. From 2010 to 2012, preeclampsia was defined as hypertension and proteinuria in accordance with the American College of Obstetricians and Gynecologists' 2002 classification.[18] Hypertension was defined as systolic blood pressure ≥140 mm Hg or diastolic blood pressure ≥90 mm Hg after 20 weeks of gestation. Proteinuria was defined as the urinary excretion of ≥0.3 g protein in a 24-hour specimen, or 0.3 g/L, or two ≥1+ readings on a dipstick in a random urine determination with no evidence of the urinary tract infection.

From 2013 to 2017, our hospital followed the American College of Obstetricians and Gynecologists Task Force Report on Hypertension in Pregnancy[10] in which proteinuria is not necessary for diagnosis when specific symptoms are present, eg, elevated liver enzymes, hematological complications, renal insufficiency, and neurological symptoms. Hypertension was classified either as new-onset hypertension after 20 weeks of gestation with blood pressure levels ≥ 140/90 mm Hg on two occasions at least 4 hours apart or as chronic hypertension.

Covariates of interest

The study investigated the following covariates to assess their potential role as confounders in the relationship between GBS diagnosis and the occurrence of preeclampsia in the study population: mother's self-report of smoking status, gestational age, self-report of parity, BMI, maternal age, herpes simplex virus (HSV), and human immunodeficiency virus (HIV). Smoking status, HSV, and HIV were treated as dichotomous variables (yes *vs.* no). Gestational age and parity were also examined as dichotomous variables: preterm birth (<37 weeks) versus full-term (≥37 weeks); nulliparous (i.e., no previous birth pregnancy) versus one previous (primiparous) or multiple previous births (multiparous). The following World Health Organization categories for BMI[19] were used: underweight (<18.5 kg/m^2), normal weight (18.5–24.9 kg/m^2) overweight (25.0–30.0 g/m^2), and obese (>30.0 kg/m^2). Given the small number of underweight women, the BMI category was combined with normal-weight women to create a trichotomous variable. Maternal age was categorized into the following four categories: (1) <20 years of age, (2) 20–29 years of age, (3) 30–39 years of age, and (4) >40 years of age. HIV was detected first by HIV 1/2 Ag/Ab Combo test (Abbott, FL), followed by confirmation of the diagnosis through a polymerase chain reaction test for HIV RNA. Herpes simplex virus diagnosis was determined either through the viral lesion culture or, if a lesion was not present but the infection was suspected, through HSV types 1– and 2–specific antibody tests.

Statistical analyses

Using the χ^2 test, we compared the distribution of the covariates between the GBS-positive and GBS-negative women

Table 1

Comparison of the distribution of demographic factors between the GBS-positive and GBS-negative pregnant women.

Demographic characteristic	GBS+ women (n = 977) *n* (%)	GBS– women (n = 7,042) *n* (%)	χ^2 (*df*)	*P*†
Smoker*				
Yes	33 (3.98)	235 (3.79)	0.08 (1)	0.783
No	796 (96.02)	5972 (96.21)		
Gestational age				
Preterm birth (<37 wks)	94 (9.62)	1707 (24.24)	105.29 (1)	<0.001
Full-term (≥37 wks)	883 (90.38)	5335 (75.76)		
Parity				
Nulliparous	326 (33.37)	2667 (37.87)	7.44 (1)	0.006
Primiparous and multiparous	651 (66.63)	4375 (62.13)		
Body mass index, kg/m^2				
Underweight and normal (<25.0 kg/m^2)	184 (18.83)	996 (14.14)	15.39 (2)	<0.001
Overweight (25.0–30.0 kg/m^2)	291 (29.79)	2152 (30.56)		
Obese (>30.0 kg/m^2)	502 (51.38)	3894 (55.30)		
Maternal age group, year				
<20	89 (9.11)	535 (7.55)	6.10 (3)	0.107
20–29	521 (53.33)	3653 (51.87)		
30–40	335 (34.29)	2547 (36.17)		
>40	32 (3.28)	307 (4.36)		
HSV				
Positive	58 (5.94)	185 (2.63)	31.98 (1)	<0.001
Negative	919 (94.06)	6857 (97.37)		
HIV				
Positive	15 (1.54)	58 (0.82)	4.82 (1)	0.028
Negative	962 (98.46)	6984 (99.18)		

*Sample size lower because of missing numbers.

†*P* values obtained from χ^2 test for differences in the proportions of the covariates.

df: Degrees of freedom; GBS: group B Streptococcus; HSV: Herpes simplex virus.

Table 2

Crude and adjusted odds ratios of the relationship between GBS infection and preeclampsia.

Model of Statistical Analysis	Odds Ratio (95% *CI*)
Crude model	
GBS positive	0.46 (0.31–0.67)
GBS negative	Referent
Adjusted model	
GBS positive	0.47 (0.32–0.70)
GBS negative	Referent
Covariates in the adjusted model	
Body mass index, kg/m^2	
Underweight and normal (<25.0)	Referent
Overweight (25.0–30.0)	0.85 (0.61–1.19)
Obese (>30.0)	1.31 (1.05–1.63)
Age group, year	
<20	Referent
20–29	0.91 (0.65–1.29)
30–40	0.76 (0.53–1.09)
>40	0.82 (0.47–1.44)
HSV	
Positive	0.22 (0.07–0.68)
Negative	Referent

CI: confidence interval; GBS: group B Streptococcus; HSV: herpes simplex virus.

to determine whether there were differences. We used logistic regression to estimate the size of the association between GBS at delivery and the outcome of preeclampsia. The 10% change in estimate criterion was first used to identify potential confounders from our list of covariates. Additional covariates were selected using backward selection ($P < 0.25$) for inclusion in the adjusted logistic regression model. The results were reported as odds ratios with the corresponding 95% confidence intervals (*CI*). A *P* value less than 0.05 was considered statistically significant. Data analysis was performed using SAS on Demand for Academics (SAS Institute, Inc., New York, NY).

Ethical approval

We conducted our study in compliance with recognized international standards, including the principles of the *Declaration of Helsinki*. The institutional review board of SUNY Downstate Health Sciences University, University Hospital of Brooklyn Downstate, approved this retrospective chart review (IRB approval # 973453-1) and waived the requirement to obtain written informed consent because this study was only with no more than minimal risk and it would be impracticable to do the study if informed consent and authorization were required.

Results

After applying our inclusion and exclusion criteria, the study population was comprised of 8,019 Black women. Approximately 12% of Black women were positive for GBS ($n = 977$). The distribution of smoking status, and maternal age, were similar between the GBS-positive and-negative women ($P = 0.783$ and $P = 0.107$ respectively). The GBS-positive women were less likely to have a preterm birth (9.62% *vs.* 24.24%, $P < 0.001$) compared with the GBS-negative women. They were also less likely to be nulliparous (33.37% *vs.* 37.87%, $P = 0.006$) and to be obese (51.38% *vs.* 55.30%, $P < 0.001$). However, GBS-positive women were more likely to be positive for HSV (5.94% *vs.* 2.63%, $P < 0.001$) and HIV (1.54% *vs.* 0.82%, $P = 0.028$) (Table 1).

Next, we explored whether GBS is associated with the outcome of preeclampsia in this population of Black women (Table 2). The GBS-positive women had 54% reduced odds of having a preeclampsia diagnosis (odds Ratio, 0.46; 95% *CI*, 0.31–0.67) than the GBS-negative women. None of the covariates met the criteria for confounding based on the 10% change-in-estimate criterion. Therefore, we selected covariates for the model based on the backward selection method using a *P* value for selection of $P < 0.250$ (only BMI, maternal age, and diagnosis of HSV met the criteria). After adjustment for these covariates, the relationship was slightly attenuated. The GBS-positive women had 53% reduced odds of being diagnosed with preeclampsia (odds ratio, 0.47; 95% CI, 0.32–0.70).

Discussion

Our study found that Black women, diagnosed with GBS, had 53% reduced odds of receiving a diagnosis of preeclampsia compared with women who were GBS-negative in a cohort of Black women without hypertensive or diabetic comorbidities. The findings from our cross-sectional study are consistent with another cross-sectional study performed by Mulla *et al.*[7] that assessed the relationship between GBS diagnosis and preeclampsia in two cohorts of women in Florida and Texas. However, these findings should be interpreted with caution as these results were unable to be replicated when Mulla *et al.*[8] (2015) repeated their earlier 2013 study using the stronger case-control study design or the study by Edwards *et al.*[9] (2019) that used the more reliable retrospective cohort study design. Both of these designs provide stronger evidence for inferring causality. Race and ethnicity may contribute to the discrepancy between our findings and the others' reports. In the studies cited, the proportion of Black patients ranged from 1.5% to 35%, whereas our study utilized data from an entirely Black population. Our previous study in the Black population indicated that preeclampsia-related systemic inflammation was differentially activated than those reported in the other races.[17] Thus, the inflammation phenotype in Black preeclampsia patients may be different than those in the other races. Such an immune background may respond to GBS differently in Black patients, which inadvertently affects preeclampsia development.

It has been speculated that immune regulation of the maternal-fetal interface is the result of the coordinated interaction between all its cellular components, including bacteria.[20] Accumulative evidence has indicated potential links of GBS colonization with maternal/placental changes at cellular and molecular levels. Experimental studies showed that GBS inhibits autophagy in vaginal epithelial cells,[21] causing vaginal epithelial exfoliation, which facilitates spreading of infection to the uterus.[22] Group B Streptococcus also activates transcriptomic pathways related to premature birth in the human extraplacental membranes.[23] Group B Streptococcus induces the expression of human β-defensin-2 in human extraplacental membrane[24] and secretion of maternal and placental cytokines, such as IL-1β, CXCL1, MMP-10,[25,26] IL-1 receptor antagonist,[27] and IL-10.[28] Neutrophils respond to GBS by producing extracellular traps,[29] which may be circumvented during GBS amniotic cavity invasion to induce fetal injury and preterm labor.[30] Human placental

macrophages respond to GBS by releasing macrophage extracellular traps,[31] possibly through activation of protein kinase D.[32] Decidual stromal cell-derived PGE2 regulates these macrophage responses.[33] Mast cells respond to GBS by degranulation, leading to the release of preformed and pro-inflammatory mediators,[34] such as chymotrypsin-like cleavage specificity in response to GBS.[35] These maternal/placental changes by GBS at cellular and molecular levels may affect the development of preeclampsia. One potential mechanism is that GBS colonization triggers a maternal immune response, which may involve the activation of inflammatory cells and release of inflammatory cytokines or mediators. These alterations in inflammatory phenotype due to GBS colonization may modulate the sterile inflammation induced by other mechanisms in preeclampsia.[36] Thus, infection-induced inflammation may correct the noninfection-induced inflammation, unintentionally mitigating the development of preeclampsia.

Our study identified a lower prevalence of GBS (12%) compared with the reported U.S. figure, approximately 19%.[3] A major strength of our study was the ability to investigate this relationship in a Black population, avoiding potential confounding effects related to hypertensive and diabetic comorbidities. However, this study is limited in confirming whether the study population received prophylaxis treatment earlier in pregnancy, which could introduce bias in the interpretation of the role of the immune response. For example, we found that GBS-positive patients were also more likely to be positive for other infections such as HSV, whereas preeclamptic women were less likely to have GBS or HSV. Given the nature of preeclampsia, it is plausible that preeclamptic women would be more likely to have received antibiotic prophylaxis and thus less likely to have untreated infections at delivery. In addition, the temporal association is unable to be verified in this cross-sectional design because it did not allow for the exploration of whether the GBS colonization occurred before the development of preeclampsia. Future research should identify a cohort earlier in pregnancy to better establish the temporal relationship between GBS exposure and preeclampsia as well as address the potential for bias from antibiotic prophylaxis.

Conclusion

Our study discovered a reduced likelihood of preeclampsia among Black women who were positive for GBS at delivery. Further research is needed to explore this association.

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Author Contributions

Keun Soo Kwon, Ming Zhang, Ivan Velickovic, Mudar Dalloul, and David Wlody did the study design and manuscript preparation. Keun Soo Kwon, Tzu Hsuan Cheng, Simone A. Reynolds, Jordan Zhou, Huchong Cai, Sharon Lee, and Ming Zhang did the data collection and analyses.

Conflicts of Interest

None.

Data Availability

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

References

[1] Bianchi-Jassir F, Seale AC, Kohli-Lynch M, et al. Preterm birth associated with group B Streptococcus maternal colonization worldwide: systematic review and meta-analyses. Clin Infect Dis 2017;65(suppl 2):S133–S142. doi: 10.1093/cid/cix661.

[2] Armistead B, Oler E, Adams Waldorf K, et al. The double life of group B Streptococcus: asymptomatic colonizer and potent pathogen. J Mol Biol 2019;431(16):2914–2931. doi: 10.1016/j.jmb.2019.01.035.

[3] Kwatra G, Cunnington MC, Merrall E, et al. Prevalence of maternal colonisation with group B streptococcus: a systematic review and meta-analysis. Lancet Infect Dis 2016;16(9):1076–1084. doi: 10.1016/S1473-3099(16)30055-X.

[4] Russell NJ, Seale AC, O'Driscoll M, et al. Maternal colonization with group B Streptococcus and serotype distribution worldwide: systematic review and meta-analyses. Clin Infect Dis 2017;65(suppl 2):S100–S111. doi: 10.1093/cid/cix658.

[5] Kobayashi M, Schrag SJ, Alderson MR, et al. WHO consultation on group B Streptococcus vaccine development: report from a meeting held on 27–28 April 2016. Vaccine 2019;37(50):7307–7314. doi: 10.1016/j.vaccine.2016.12.029.

[6] Oseghale O, Vlahos R, O'Leary JJ, et al. Influenza virus infection during pregnancy as a trigger of acute and chronic complications. Viruses 2022;14(12):2729. doi: 10.3390/v14122729.

[7] Mulla ZD, Annavajjhala V, Gonzalez-Sanchez JL, et al. Group B streptococcal colonization and the risk of pre-eclampsia. Epidemiol Infect 2013;141(5):1089–1098. doi: 10.1017/S0950268812001598.

[8] Mulla ZD, Carrillo T, Kalamegham R, et al. Is maternal colonization with group B streptococci a risk factor for preeclampsia? J Reprod Med 2015;60(3–4):117–126.

[9] Edwards JM, Watson N, Focht C, et al. Group B Streptococcus (GBS) colonization and disease among pregnant women: a historical cohort study. Infect Dis Obstet Gynecol 2019;2019:5430493. doi: 10.1155/2019/5430493.

[10] Bibbins-Domingo K, Grossman DC, Curry SJ, et al. Screening for preeclampsia: US preventive services task force recommendation statement. JAMA 2017;317(16):1661–1667. doi: 10.1001/jama.2017.3439.

[11] Savitz DA, Danilack VA, Engel SM, et al. Descriptive epidemiology of chronic hypertension, gestational hypertension, and preeclampsia in New York state, 1995-2004. Matern Child Health J 2014;18(4):829–838. doi: 10.1007/s10995-013-1307-9.

[12] Valkenburg-van den Berg AW, Sprij AJ, Oostvogel PM, et al. Prevalence of colonisation with group B streptococci in pregnant women of a multi-ethnic population in The Netherlands. Eur J Obstet Gynecol Reprod Biol 2006;124(2):178–183. doi: 10.1016/j.ejogrb.2005.06.007.

[13] Gopal Rao G, Hiles S, Bassett P, et al. Differential rates of group B streptococcus (GBS) colonisation in pregnant women in a racially diverse area of London, UK: a cross-sectional study. BJOG 2019;126(11):1347–1353. doi: 10.1111/1471-0528.15648.

[14] Spiel MH, Hacker MR, Haviland MJ, et al. Racial disparities in intrapartum group B Streptococcus colonization: a higher incidence of conversion in African American women. J Perinatol 2019;39(3):433–438. doi: 10.1038/s41372-018-0308-3.

[15] Centers for Disease Control and Prevention (CDC). Trends in perinatal group B streptococcal disease—United States, 2000–2006. MMWR Morb Mortal Wkly Rep 2009;58(5):109–112.

[16] Stapleton RD, Kahn JM, Evans LE, et al. Risk factors for group B streptococcal genitourinary tract colonization in pregnant women. Obstet Gynecol 2005;106(6):1246–1252. doi: 10.1097/01.AOG.0000187893.52488.4b.

[17] Velickovic I, Dalloul M, Wong KA, et al. Complement factor B activation in patients with preeclampsia. J Reprod Immunol 2015; 109:94–100. doi: 10.1016/j.jri.2014.12.002.
[18] ACOG practice bulletin. Diagnosis and management of preeclampsia and eclampsia. Number 33, January 2002. Obstet Gynecol 2002;99 (1):159–167. doi: 10.1016/s0029-7844(01)01747-1.
[19] World Health Organization. A healthy lifestyle—who recommendations. 2010. Available at: https://www.who.int/europe/news-room/fact-sheets/item/a-healthy-lifestyle—who-recommendations. Accessed August 17, 2023.
[20] Mor G, Kwon JY. Trophoblast-microbiome interaction: a new paradigm on immune regulation. Am J Obstet Gynecol 2015;213(4 suppl): S131–S137. doi: 10.1016/j.ajog.2015.06.039.
[21] Scholl J, Nasioudis D, Boester A, et al. Group B streptococcus alters properties of vaginal epithelial cells in pregnant women. Am J Obstet Gynecol 2016;214(3):383.e1–383.e5. doi: 10.1016/j.ajog.2015.12.053.
[22] Vornhagen J, Armistead B, Santana-Ufret V, et al. Group B streptococcus exploits vaginal epithelial exfoliation for ascending infection. J Clin Invest 2018;128(5):1985–1999. doi: 10.1172/JCI97043.
[23] Park HR, Harris SM, Boldenow E, et al. Group B streptococcus activates transcriptomic pathways related to premature birth in human extraplacental membranes in vitro. Biol Reprod 2018;98(3): 396–407. doi: 10.1093/biolre/iox147.
[24] Boldenow E, Hogan KA, Chames MC, et al. Role of cytokine signaling in group B Streptococcus-stimulated expression of human beta defensin-2 in human extraplacental membranes. Am J Reprod Immunol 2015;73(3):263–272. doi: 10.1111/aji.12325.
[25] Bergeron J, Gerges N, Guiraut C, et al. Activation of the IL-1β/CXCL1/MMP-10 axis in chorioamnionitis induced by inactivated group B Streptococcus. Placenta 2016;47:116–123. doi: 10.1016/j.placenta.2016.09.016.
[26] Allard MJ, Giraud A, Segura M, et al. Sex-specific maternofetal innate immune responses triggered by group B streptococci. Sci Rep 2019; 9(1):8587. doi: 10.1038/s41598-019-45029-x.
[27] Witkin SS, Gravett MG, Haluska GJ, et al. Induction of interleukin-1 receptor antagonist in rhesus monkeys after intraamniotic infection with group B streptococci or interleukin-1 infusion. Am J Obstet Gynecol 1994;171(6):1668–1672. doi: 10.1016/0002-9378(94)90419-7.
[28] Zaga-Clavellina V, Flores-Espinosa P, Pineda-Torres M, et al. Tissue-specific IL-10 secretion profile from term human fetal membranes stimulated with pathogenic microorganisms associated with preterm labor in a two-compartment tissue culture system. J Matern Fetal Neonatal Med 2014;27(13):1320–1327. doi: 10.3109/14767058.2013.857397.
[29] Kothary V, Doster RS, Rogers LM, et al. Group B Streptococcus induces neutrophil recruitment to gestational tissues and elaboration of extracellular traps and nutritional immunity. Front Cell Infect Microbiol 2017;7:19. doi: 10.3389/fcimb.2017.00019.
[30] Boldenow E, Gendrin C, Ngo L, et al. Group B Streptococcus circumvents neutrophils and neutrophil extracellular traps during amniotic cavity invasion and preterm labor. Sci Immunol 2016;1(4):eaah4576. doi: 10.1126/sciimmunol.aah4576.
[31] Doster RS, Sutton JA, Rogers LM, et al. *Streptococcus agalactiae* induces placental macrophages to release extracellular traps loaded with tissue remodeling enzymes via an oxidative burst-dependent mechanism. mBio 2018;9(6):e02084–e02018. doi: 10.1128/mBio.02084-18.
[32] Sutton JA, Rogers LM, Dixon B, et al. Protein kinase D mediates inflammatory responses of human placental macrophages to group B Streptococcus. Am J Reprod Immunol 2019;81(3):e13075. doi: 10.1111/aji.13075.
[33] Rogers LM, Anders AP, Doster RS, et al. Decidual stromal cell-derived PGE(2) regulates macrophage responses to microbial threat. Am J Reprod Immunol 2018;80(4):e13032. doi: 10.1111/aji.13032.
[34] Gendrin C, Vornhagen J, Ngo L, et al. Mast cell degranulation by a hemolytic lipid toxin decreases GBS colonization and infection. Sci Adv 2015;1(6):e1400225. doi: 10.1126/sciadv.1400225.
[35] Gendrin C, Shubin NJ, Boldenow E, et al. Mast cell chymase decreases the severity of group B Streptococcus infections. J Allergy Clin Immunol 2018;142(1):120–129.e6. doi: 10.1016/j.jaci.2017.07.042.
[36] Banerjee S, Huang Z, Wang Z, et al. Etiological value of sterile inflammation in preeclampsia: is it a non-infectious pregnancy complication? Front Cell Infect Microbiol 2021;11:694298. doi: 10.3389/fcimb.2021.694298.

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