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Urinary Tract Infection and Progression to Pyelonephritis: Group B *Streptococcus* versus *E. coli*

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Abstract

Objective Group B *Streptococcus* (GBS) colonization of the lower urinary tract in pregnancy is associated with severe infections such as chorioamnionitis, endometritis, and pyelonephritis. The objective of this study was to compare rates of progression to pyelonephritis between GBS and *Escherichia coli* lower urinary tract infections (LUTIs), as well as compare infectious and obstetric morbidity secondary to these pathogens.

Study Design Retrospective cohort of pregnant women with LUTIs (asymptomatic bacteria or acute cystitis [AC]) from a single health system between July 2013 and May 2019. Demographic, infectious, antepartum, and intrapartum data were abstracted from medical records of women with GBS or *E. coli* LUTI. The primary outcome was progression to pyelonephritis. Secondary outcomes included pyelonephritis-related anemia, sepsis, pyelonephritis length of stay (LOS), median gestational age (GA) at delivery, preterm delivery, and low birth weight (LBW). Logistic regression was used to calculate the adjusted odds of the primary outcome.

Results Of 729 pregnant women with urinary colonization, 433 were culture positive for one of the aforementioned bacteria, with 189 (43.6%) having GBS and 244 (56.4%) having *E. coli*. Women with *E. coli* were more likely to be younger, use tobacco, have a history of AC, and have a history of preterm birth. Rates of progression to pyelonephritis were markedly higher with *E. coli* (15.6%) than with GBS (1.1%; $p < 0.001$). Median LOS for pyelonephritis and pyelonephritis-related morbidities did not differ. Median GA at delivery, preterm delivery, and LBW rates also did not differ. In adjusted analysis, controlling for history of AC, insurance status, tobacco use, prior preterm birth, primary infection type, and maternal age, women with GBS LUTI had markedly decreased odds of developing pyelonephritis in pregnancy compared with those with *E. coli* (adjusted odds ratio: 0.04, 95% confidence interval: 0.01–0.28).

Conclusion *Escherichia coli* infections progress to pyelonephritis in pregnancy at markedly higher rates than GBS, although obstetric outcomes are similar.

Keywords
- acute cystitis
- asymptomatic bacteriuria
- *E. coli*
- GBS
- pregnancy
- pyelonephritis
- pyelonephritis-related morbidity
- urinary tract infection
- uropathogens

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Lower urinary tract infections (LUTIs) are the most common infection in pregnancy, occurring in 5 to 10% of all pregnancies.[1] LUTIs may be classified as asymptomatic bacteriuria (ASB) or acute cystitis (AC). Both ASB and AC have been associated with increased risk of pyelonephritis in pregnancy. Acute pyelonephritis affects 1 to 2% of pregnant women, and has been associated with increased rates of preeclampsia, preterm labor, sepsis, and low birth weight (LBW).[2,3]

Escherichia coli is the most common organism associated with symptomatic and asymptomatic LUTI, found in 65 to 84% of pregnant women.[4] Another common uropathogen of pregnancy is group B *Streptococcus* (GBS), which is found in 2 to 10% of ASB cultures.[1] Vaginal colonization with GBS is associated with increased risk of premature rupture of membranes, preterm labor, and neonatal sepsis. Additionally, GBS is the primary uropathogen in approximately 10% cases of pyelonephritis in pregnancy.[5] However, less is known about the risk of progression to pyelonephritis and the severity of the pyelonephritis when caused by GBS.[5] Thus, the objective of this study was to evaluate if the rate at which GBS colonization progresses to pyelonephritis is different from the rate at which the more common uropathogen, *E. coli*, progresses to pyelonephritis, and compare how colonization with these two organisms affects pyelonephritis-related morbidity and obstetric outcomes.

Methods

This was a retrospective cohort study of all pregnant women presenting to a single health care system with LUTI, including ASB or AC, from the first trimester of pregnancy through 6 weeks postpartum (Institutional Review Board: Pro00101602 Approved February 20, 2019). Women delivering at a Duke University-affiliated hospital from July 1, 2013, to May 1, 2019, were included. Eligible patients were identified using International Classification of Diseases, 9th (ICD-9) and 10th (ICD-10) revision codes for ASB, AC, and pyelonephritis and culture data (►**Supplementary Table 1**, available in the online version). For this study, we defined pyelonephritis as coded by ICD-9 or ICD-10 code. Then, to be included in the study, patients needed to have a clinical diagnosis of pyelonephritis documented in the medical record, including documentation of UTI symptoms, with flank pain and/or fevers. All patients were treated with antibiotics to which they were sensitive per institution protocol.

Women with a urine culture that grew *E. coli* or GBS and who delivered in a single health care system were included. Women who had one single culture come back positive for both organisms, *E. coli* and GBS, or who had a urine culture that grew out a different uropathogen were also excluded. The primary infection type was defined as ASB or AC and was defined as urine culture positive for a single organism with 10^5 cfu/mL or greater and 10^2 cfu/mL or greater without or with symptoms, respectively.[4] Asymptomatic women with urine cultures less than 10^5 cfu/mL were excluded. Demographic variables, antepartum and pregnancy complications, delivery, and postpartum data were collected via review of the electronic medical record by trained chart abstractors.

The primary outcome was pyelonephritis, defined clinically by fever at or above 38.0°C, flank pain, and a positive urine culture. Secondary outcomes included length of stay (LOS) for pyelonephritis admission, median gestational age (GA) at delivery, preterm delivery (PTD), LBW, and pyelonephritis-related complications, including renal abscess, sepsis, and pyelonephritis-related anemia. PTD was defined as delivery prior to $37^{0/7}$ weeks. LBW was defined based on GA-specific national norms.[6] Pyelonephritis-related anemia was defined as a hematocrit of less than 33 identified at the time of pyelonephritis diagnosis, in the setting of a prior normal hematocrit.[7]

Baseline demographics were analyzed using bivariate analysis. Continuous, normally distributed variables were compared using Student's *t*-test, while nonparametric continuous variables were compared using Wilcoxon's rank-sum tests. Categorical variables were analyzed using chi-square tests or Fisher's exact tests as appropriate. Multivariate logistic regression was used to determine significant predictors of the primary outcome. Statistical significance was defined as *p*-value less than 0.05. Statistical analysis was performed using STATA software.

Results

Of 729 pregnant women with urinary colonization information in the study period, 433 grew one of the bacteria of interest, with 189 (43.6%) being culture positive for GBS and 244 (56.4%) being culture positive for *E. coli* (►**Fig. 1**).

Women with *E. coli* were younger and less likely to have private insurance (►**Table 1**). Women with *E. coli* were also more likely to use tobacco, to have a prior history of AC before this pregnancy and have AC in this pregnancy (►**Table 1**). Prior preterm birth was also twice as common among women with *E. coli* than women with GBS (21.0 vs. 10.6%, $p < 0.01$). Other baseline demographics, including GA at first infection did not differ, and are seen in ►**Table 1**. Median duration of antibiotic treatment did not differ by uropathogen (7 days with interquartile range 7, 7 for both, $p = 0.69$).

Rates of progression to pyelonephritis were markedly higher with *E. coli* LUTI than with GBS (15.6 vs. 0.50%; $p < 0.01$). However, LOS during the admission for pyelonephritis did not differ (►**Table 2**). Pyelonephritis-related morbidity was rare in both groups. There was no difference between time from positive culture to diagnosis of pyelonephritis between the *E. coli* and GBS groups (►**Table 2**). No women in either group had an intrauterine fetal demise, and only one patient (*E. coli* group) delivered during the admission for pyelonephritis. Similarly, only one patient (*E. coli* group, though different than the one who delivered during her pyelonephritis admission) went to the intensive care unit (ICU). This patient also received a blood transfusion. Anemia and hematocrit nadir also did not differ by infectious agent (►**Table 2**).

Obstetric outcomes, including median GA at delivery, preterm delivery, and LBW rates, did not differ (►**Table 2**).

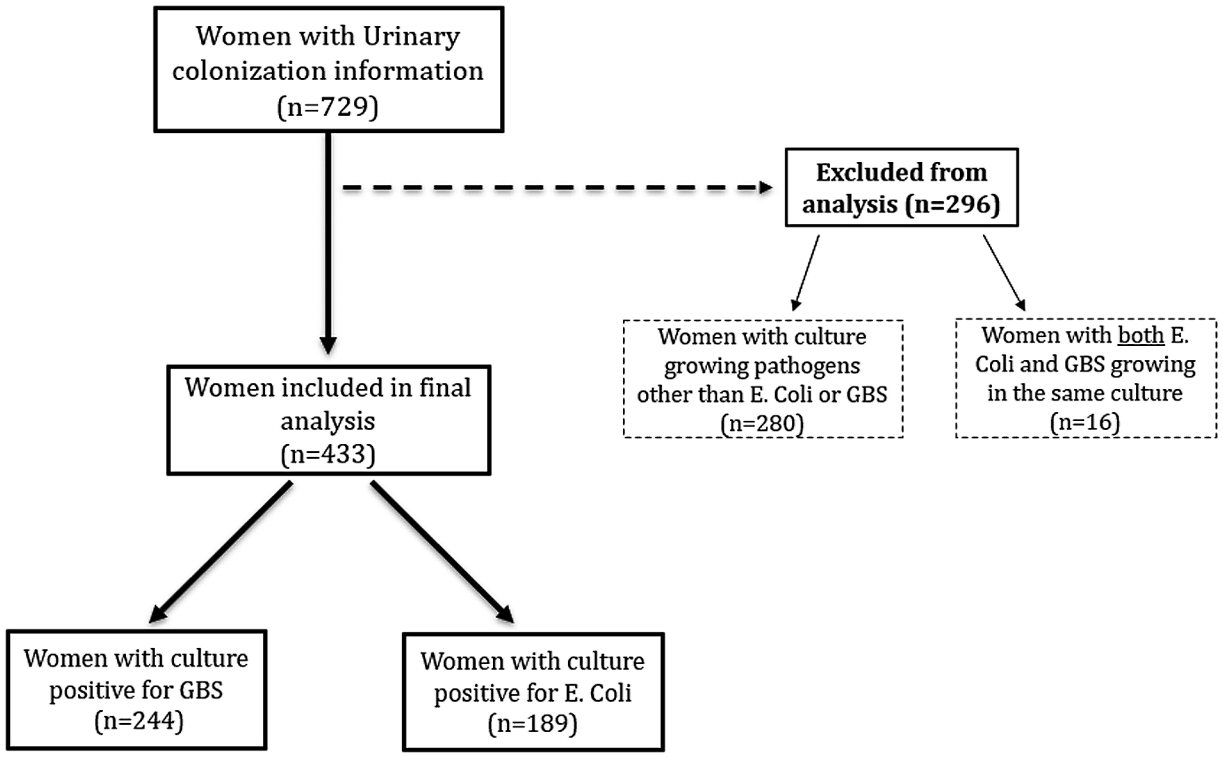

Fig. 1 Study population. GBS, group B *Streptococcus*.

Table 1 Maternal demographics among with GBS or *E. coli* lower urinary tract infection

	E. coli $n = 244$ (%)	GBS $n = 189$ (%)	*p*-Value
Median age, y (IQR)	26 (22, 31)	28 (23, 33)	< 0.01
African American race	54 (22.1)	44 (23.3)	0.78
Private insurance	66 (27.5)	71 (38.6)	0.02
Limited prenatal care	13 (5.4)	13 (7.1)	0.48
Chronic hypertension	21 (8.6)	14 (7.4)	0.65
Diabetes mellitus	17 (7.0)	9 (4.8)	0.34
Sickle cell trait	16 (6.6)	13 (6.9)	0.91
Tobacco use	42 (17.2)	13 (6.9)	< 0.01
Median baseline hematocrit (IQR)	36.7 (34.0, 38.7)	37.0 (35.3, 39.6)	0.05
Multiparous	150 (61.5)	127 (67.2)	0.22
Prior preterm birth	51 (21.0)	20 (10.6)	< 0.01
History of AC	79 (32.4)	24 (12.7)	< 0.01
GA of first infection	12.1 (9.3, 18.4)	11.2 (8.9, 19.3)	0.49
First infection: UTI	63 (26.8)	19 (10.2)	< 0.01

Abbreviations: AC, acute cystitis; GA, gestational age; GBS, group B *Streptococcus*; IQR, interquartile range; UTI, urinary tract infection.

When controlling for history of AC, black race, insurance status, tobacco use, prior preterm birth, primary infection type, and maternal age, women with GBS LUTI had markedly decreased odds of progressing to pyelonephritis compared with those with *E. coli* LUTI (adjusted odds ratio: 0.06, 95% confidence interval: 0.01–0.53).

Comment

Principal Findings

Women with an *E. coli* LUTI were significantly more likely to progress to pyelonephritis than women with cultures positive for GBS. However, other pyelonephritis-related and obstetric morbidities did not differ.

Table 2 Pyelonephritis-related and obstetrics outcomes among with GBS or *E. coli* lower urinary tract infection

	E. coli $n = 244$ (%)	GBS $n = 189$ (%)	*p*-Value
Progression to pyelonephritis	38 (15.6)	1 (0.50)	< 0.001
Median time from positive culture to pyelonephritis diagnosis, wk (IQR)	16.6 (9.6, 22.3)	17.2 (–)	0.79
Median GA at pyelonephritis diagnosis (IQR)	25.6 (19.7, 32.1)	21.6 (–)	0.56
Median pyelonephritis LOS (IQR)	3 (2, 4)	3 (–)	0.89
Median hematocrit nadir (IQR)	30 (26.3, 32.7)	30.3 (–)	0.79
Anemia	27/38 (71.1)	1/1 (100)	0.53
Sepsis	3/38 (7.9)	0/1	0.68
Median GA at delivery, wk (IQR)	39.1 (37.6, 40.1)	39.4 (38.6, 40.1)	0.07
Preterm birth	30 (12.3)	16 (8.5)	0.20
Low birth weight	21 (8.6)	21 (11.1)	0.38

Abbreviations: GA, gestational age; GBS, group B *Streptococcus*; IQR, interquartile range; LOS, length of stay.

Results

Previous studies have found *E. coli* to have a higher rate of progression to pyelonephritis when compared with other organisms, such as GBS, *Klebsiella*, and *Proteus*.[8] However, data related to the morbidity associated with specific uropathogens is not well described in the literature. As pyelonephritis-related morbidities are rare, it is challenging to identify a dataset with enough detail to drill down to the level of the urinary pathogens, but large enough to be powered to show specific pyelonephritis-related morbidities. Despite the difference in progression, rates of pyelonephritis-related morbidity and obstetric outcomes between *E. coli* and GBS in this study did not differ. Due to the physiologic changes in pregnancy, pyelonephritis during this time is associated with higher maternal risks than this infection outside of pregnancy. Thus, it is physiologically plausible that it is not the pathogen which causes the morbidity, but the specific physiologic changes themselves. Other authors have shown similarly that more pathogenic infections are also not associated with differences in pyelonephritis-related morbidities, adding validity to this theory.[9]

Clinical Implications

Pyelonephritis is the most common infectious cause of hospitalization in pregnancy and has been associated with severe maternal morbidity. Women with pyelonephritis during delivery have been found to have increased odds of pulmonary edema, acute respiratory distress syndrome, conditions leading to transfusion and mechanical ventilation, and end-organ failure compared with women without pyelonephritis.[10] More severe infections, including sepsis and chorioamnionitis were also more likely to occur among women with pyelonephritis.[10] In this study, severe morbidity including ICU admission, transfusion, and sepsis was rare, though it did occur with higher frequency in the *E. coli* group.

Though GBS is such a common vaginal pathogen with major neonatal and fetal implications, little attention has been paid to the maternal impact of GBS infections. Vaginal GBS cultured in pregnancy and the postpartum period has been associated with chorioamnionitis, mastitis, bacteremia, sepsis, and wound infections. GBS has also been implicated as the sole pathogen in 2 to 14% of endometritis and was more likely to be isolated after vaginal deliveries than cesarean deliveries.[11] These infections have been documented to have life-threatening maternal sequelae, including peritonitis and pelvic abscesses, underscoring the importance of not minimizing GBS infections.[11] Though the risks of progression to pyelonephritis is low when compared with *E. coli*, pyelonephritis due to any bacteria can still have maternal, obstetric, and neonatal implications, thus emphasizing the importance of treating GBS LUTI.

Research Implications

As pyelonephritis-related morbidities are uncommon, larger studies are needed to better examine the risks of these as they relate to specific urinary pathogens. Similarly, given the overall low number of women with pyelonephritis, larger studies are needed to determine the true obstetric implications of GBS-related pyelonephritis. Additionally, nearly one in six women in the *E. coli* group had progression to pyelonephritis. This rate is high and warrants further consideration as to specific infection-related risk factors that lead to treatment failure and infectious progression.

Strengths and Limitations

This study has many strengths. First, based on a systematic search of the literature, it is among the larger studies to date specifically examining GBS-related pyelonephritis and comparing it to the more common pyelonephritis caused by *E. coli*. Additionally, the rate of progression to pyelonephritis in this study was similar to those previously published in the literature,[5] adding validity to our findings. There are also multiple limitations. Our total number of women with GBS-related pyelonephritis was low, thus limiting our ability to comment on morbidity related to this specifically. However, even in the *E. coli* group, morbidity was uncommon. Similarly, due to low numbers of women with pyelonephritis, we were only able to look at obstetric outcomes by urinary pathogen and not

perform a subanalysis including only those with pyelonephritis. The use of ICD-9 and ICD-10 codes for diagnosis introduces potential transition and coding errors that may disrupt the observed rates. Regarding treatment, we are unable to assess compliance unless it is documented in the medical record, and in those cases, it is dependent on patient honesty. Tests of cure could be used as a measure of compliance, but this is further limited because though they are recommended, they are not routinely performed. As with all retrospective studies, we can comment in associations but not causality. Additionally, this is retrospective data from a single health system, thus this may not be generalizable to all populations.

Conclusion

In sum, in this study, even after controlling for confounders, women with *E. coli* LUTI develop pyelonephritis at markedly higher rates than those with a GBS-related LUTI. Though larger studies are needed to collaborate these data, this should not undervalue the importance of treating GBS UTI, as any progression to pyelonephritis can be dangerous for the mother, the fetus, and the pregnancy.

Highlights

- *E. coli*-related UTI progresses to pyelonephritis at markedly higher rates than GBS-related LUTI.
- Obstetric outcomes were similar between women with *E. coli* and GBS-related LUTI.
- Maternal consequences of pyelonephritis may be severe regardless of causal urinary pathogen.

Condensation

Women with an *E. coli* lower urinary tract infection were significantly more likely to progress to pyelonephritis than women with urine cultures positive for GBS.

AJOG at a Glance

A. Why was this study conducted?

To assess if there is a difference in progression to pyelonephritis during pregnancy for *E. coli* infections versus GBS infections.

B. What are the key findings?

E. coli lower urinary tract infections progress to pyelonephritis at significantly higher rates than GBS, though obstetric outcomes were similar.

C. What does this study add to what is already known?

Urinary tract infections have higher rates of progression to pyelonephritis during pregnancy; however, differences in the rates of pyelonephritis-related morbidity for specific uropathogens have not been well studied. This study highlights a significantly higher rate of progression for *E. coli* compared with GBS, though obstetric outcomes are similar.

Note

This work was presented as a poster presentation at the Society for Maternal-Fetal Medicine's 40th Annual Pregnancy meeting in February 2020 in Dallas, TX.

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None.

Conflict of Interest

None declared.

References

1 Abou Heidar NF, Degheili JA, Yacoubian AA, Khauli RB. Management of urinary tract infection in women: a practical approach for everyday practice. Urol Ann 2019;11(04):339–346
2 Foxman B. Epidemiology of urinary tract infections: incidence, morbidity, and economic costs. Am J Med 2002;113(Suppl 1A): 5S–13S
3 Kalinderi K, Delkos D, Kalinderis M, Athanasiadis A, Kalogiannidis I. Urinary tract infection during pregnancy: current concepts on a common multifaceted problem. J Obstet Gynaecol 2018;38(04): 448–453
4 Nicolle LE. Asymptomatic bacteriuria and bacterial interference. Microbiol Spectr 2015;3(05):
5 Allen VM, Yudin MH. No. 276-management of group B streptococcal bacteriuria in pregnancy. J Obstet Gynaecol Can 2018;40 (02):e181–e186
6 Olsen IE, Groveman SA, Lawson ML, Clark RH, Zemel BS. New intrauterine growth curves based on United States data. Pediatrics 2010;125(02):e214–e224
7 ACOG Practice Bulletin No. 95: anemia in pregnancy. Obstet Gynecol 2008;112(01):201–207
8 Hill JB, Sheffield JS, McIntire DD, Wendel GD Jr. Acute pyelonephritis in pregnancy. Obstet Gynecol 2005;105(01):18–23
9 Rosett HA, Krischak MK, Sachdeva S, et al. Lower urinary pathogens: do more pathogenic bacteria increase the risk of pyelonephritis? Am J Perinatol 2022;39(05):473–478
10 Dotters-Katz SK, Heine RP, Grotegut CA. Medical and infectious complications associated with pyelonephritis among pregnant women at delivery. Infect Dis Obstet Gynecol 2013:124102
11 Muller AE, Oostvogel PM, Steegers EA, Dörr PJ. Morbidity related to maternal group B streptococcal infections. Acta Obstet Gynecol Scand 2006;85(09):1027–1037