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THE BRASS TACKS: CONCISE REVIEWS OF PUBLISHED EVIDENCE

Antibiotics for culture-positive asymptomatic bacteriuria in pregnant women can prevent pyelonephritis

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NNT color recommendation	Green (benefits > harms)
Summary heading	Antibiotics for culture-positive asymptomatic bacteriuria in pregnant women can prevent pyelonephritis
Benefits in NNT	1 in 7 were helped (pyelonephritis prevented) 1 in 9 were helped (preterm birth prevented) 1 in 20 were helped (low birthweight prevented)
Benefits in percentages	15% lower risk of pyelonephritis 11% lower risk of preterm birth 5% lower risk of neonates with low birthweight
Harms in NNT (NNH)	Not reported
Harms in percentages	Not reported
Efficacy endpoints	Rates of pyelonephritis, preterm birth, low birthweight
Harm endpoints	Maternal side effects
Who was in the studies	Pregnant women in all three trimesters of pregnancy in 12 studies (*N* = 2,017)

NARRATIVE

Asymptomatic bacteriuria, occurring in 2% TO 15% of pregnancies, is generally defined as at least one urine culture showing >100,000 colony-forming units (CFUs)/mL in the absence of fever or symptoms of urinary tract infection.[1] *Escherichia coli* is the most commonly associated pathogen, comprising up to 80% of isolates.[2] While asymptomatic bacteriuria in nonpregnant women is generally benign, in pregnant women there is an increased likelihood for progression to pyelonephritis likely due to mechanical compression of the ureters by an enlarged uterus as well as smooth muscle relaxation induced by progesterone.[3] Some studies suggest that if asymptomatic bacteriuria is left untreated, up to 30% of pregnant women will develop acute pyelonephritis,[4] which may be associated with potentially serious maternal complications such as sepsis[5] and pregnancy outcomes such as low birthweight and preterm birth.[6]

The systematic review summarized here included 2,017 pregnant women from 12 randomized controlled trials that compared antibiotic treatment of asymptomatic bacteriuria to placebo or no treatment. [7] Most of the women were enrolled through prenatal screening in hospital-based clinics, and the studies included women in all stages of pregnancy. The definition of pyelonephritis varied across studies but mainly encompassed women with flank tenderness and fever, with or without urinary symptoms (such as frequency, dysuria, and hematuria) and >100,000 CFUs/mL urine. The incidence of pyelonephritis ranged from 2.2% to 36%. Included studies were performed in the 1960s through the 1980s, and study antibiotics included sulfa drugs, tetracycline, methenamine, nalidixic acid, nitrofurantoin, and ampicillin. Duration of treatment varied including single-dose, short-course (3 to 7 days), intermediate-course (3 to 6 weeks), and continuous antibiotic until delivery.

Compared to placebo or no treatment (in 11 studies of 1,932 subjects) antibiotic treatment reduced the incidence of pyelonephritis (relative risk [RR] = 0.2, 95% confidence interval [CI] = 0.1 to 0.4, absolute risk difference [ARD] = 15%, number needed to treat [NNT] = 7). Data from three studies (*n* = 327) also found that antibiotic treatment reduced the incidence of preterm birth (gestational

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age < 37 weeks; RR = 0.3, 95% CI = 0.1 to 0.9, ARD = 11%, NNT = 9). Finally, data from six studies (n = 1,437) found that antibiotics also decreased the incidence of birthweight < 2500 g (RR = 0.6, 95% CI = 0.5 to 0.9, ARD = 5%, NNT = 20).

CAVEATS

The findings of this review suggest a potentially important, clinically meaningful benefit with the use of antibiotics for asymptomatic bacteriuria in pregnancy. The underlying data, however, are heterogeneous, rife with potential systematic bias, and mostly generated 40 to 60 years ago.

The wide variation in pyelonephritis incidence among studies (2%–36%), for instance, may partially originate from the variability in definitions of pyelonephritis, or patient level characteristics such as infecting organisms, socioeconomic status, and prenatal care. Regardless of source, this variation in baseline risk introduces major clinical heterogeneity and reduces the applicability of results. Moreover, the lack of consistent blinding (four studies were double-blinded) and the significant heterogeneity across studies led the review authors to judge the quality of evidence as low. It is, in addition, difficult to confidently attribute the development of pyelonephritis to asymptomatic bacteriuria. Similarly, data on the incidence of preterm birth and low birthweight were also deemed low quality, again due to lack of blinding, heterogeneity, and small sample size. Another important weakness is the lack of reporting on maternal side effects, making it impossible to characterize the potential for adverse events in the treatment group.

In summary, although antibiotics may reduce the risk of pyelonephritis in pregnancy, as well as preterm birth and low birthweight, the evidence for treatment of asymptomatic bacteruria is low quality. More robust research is needed, particularly in a contemporary milieu, using standardized treatment protocols and stratification for baseline risk. Despite limitations, however, the data suggest significant benefit in preventing pyelonephritis, preterm birth, and low birthweight. Based on these findings it seems likely that benefits outweigh harms. It should be emphasized that this signal of benefit is based on a definition of asymptomatic bacteriuria that requires a positive urine culture, not simply a suggestive urinalysis. We would expose many more pregnant women to unclear harms for reduced benefit if we do not adhere to the clinical definition of asymptomatic bacteriuria. Therefore, we have rated antibiotic treatment for culture-positive asymptomatic bacteriuria during pregnancy as green (benefit > harms).

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