



## Editorial

## Do pregnant women with asymptomatic bacteriuria need treatment?



The April issue of the *Taiwanese Journal of Obstetrics and Gynecology* has published a very interesting article entitled “Asymptomatic pyuria in pregnant women during the first trimester is associated with an increased risk of adverse obstetrical outcomes” [1]. Lai and colleagues evaluated the outcomes of 1187 singleton pregnant women who were diagnosed with ( $n = 253$ ) and without ( $n = 934$ ) pyuria in the first trimester prenatal visit and found that women with pyuria had a significantly increased risk of preterm labor (defined by delivery before 36 gestational weeks) with odds ratio [OR] of 2.23 (95% confidence interval [CI] 1.23–4.06), compared to those pregnant women without pyuria [1]. In addition, pregnant women with pyuria also had a significantly higher risk of premature preterm rupture of membranes (OR 4.27, 95% CI 1.63–11.18), lower-birth-weight neonates (OR 1.76, 95% CI 1.04–2.97), and lower Apgar scores (OR 4.89, 95% CI 1.80–13.25) than those women without pyuria did [1]. Based on the above findings, the authors highlighted the value of screening for bacteriuria in early pregnancy and further highly recommended the need of urine cultures for these pregnant women with asymptomatic pyuria; and of most importance, the authors strongly suggested that these women should be treated with aggressive antibiotic therapy [1]. Unfortunately, the authors did not discuss the treatment strategy, such as drugs, dose, time, and duration. In addition, the authors did not consider the benefits and risks about their suggestion (screening vs. no screening, antibiotic use vs. no use, and different screening methods). Moreover, the authors failed to discuss the cost and effects of the using urine culture for these women with asymptomatic bacteriuria.

The results of current study [1] confirmed the old concept that pregnant women with undetected asymptomatic bacteriuria might be more like to have premature delivery or low-birth-weight neonates compared with those without infection [2]. However, it is still uncertain whether these pregnant women with asymptomatic bacteriuria will be beneficial for the obstetric outcomes with treatment, because the effect of treatment was less clear so far, and the response to antibiotics remains inconclusive [3]. In addition, the association of asymptomatic bacteriuria and adverse obstetric outcomes is not always consistent, and some did not show any association between two [3].

Compared with conflicted data to adverse obstetric outcomes in pregnant women with asymptomatic bacteriuria, there is relatively consistent that pregnant women with untreated asymptomatic bacteriuria had a 20–30% risk of developing pyelonephritis in later pregnancy [3]. If asymptomatic bacteriuria could be identified early in the course of the pregnancy and treated with appropriate antibiotics, the risk of pyelonephritis could be reduced by 80% [3]. Based on this observation, screening for asymptomatic bacteriuria in the

first trimester and treatment with positive women to prevent pyelonephritis becomes a standard practice in developed countries [2], including Taiwan [1]. However, there are still some, such as the Netherlands, which never considered the screening and treatment of pregnant women for asymptomatic bacteriuria as a standard practice [4]. The main cause is deficient of strong evidence to support the benefits of the screening and treatment for these pregnant women with asymptomatic bacteriuria.

The recent high-quality prospective randomized controlled trials showed the proportion of women with pyelonephritis, preterm birth, or both did not differ between untreated or placebo-treated asymptomatic bacteriuria-positive women and asymptomatic bacteriuria-negative women (2.9% [6/208] vs. 1.9% [77 of 4035]; adjusted OR 1.5, 95% CI 0.6–3.5) nor between asymptomatic bacteriuria-positive women treated with nitrofurantoin vs. those who were untreated or received placebo (2.5% [1 of 40] vs. 2.9% [6 of 208]; risk difference  $-0.4$ , 95% CI  $-3.6$  to  $9.4$ ) [4]. Five of 208 untreated or placebo-treated asymptomatic bacteriuria-positive women developed pyelonephritis compared with 24 of 4035 asymptomatic bacteriuria-negative women did (2.4% vs. 0.6%, adjusted OR 3.9, 95% CI 1.4–11.4). Taken together, the study did not support the old concept that symptomatic bacteriuria is associated with preterm birth, but supported that asymptomatic bacteriuria indeed had a significantly increased risk of pyelonephritis [4]. Even though the strong association between asymptomatic bacteriuria and pyelonephritis, the authors did not favor the concept— a routine screen-treat-policy for asymptomatic bacteriuria in pregnancy to current health care settings, because the absolute risk of pyelonephritis in untreated asymptomatic bacteriuria is low [4].

The negative impact of maternal urinary tract infection on newborns was also questioned by epidemiology study. One study enrolled mothers of 989 infants born before 28 gestational weeks who were interviewed about urine, bladder, or kidney infections (urinary tract infections) and cervical or vaginal infections (genital tract infections) during pregnancy, and found that infants born to women who reported a urinary tract infection were less likely than were others to have a very low Mental Development Index (adjusted OR 0.5, 95% CI 0.3–0.8), whereas infants born to women who reported a genital tract infection were more likely than others to have a low Psychomotor Development Index (adjusted OR 1.7, 95% CI 1.04, 2.7) [5]. In this high-risk sample, maternal gestational genital tract infection, but not urinary tract infection, was associated with a higher risk of impaired motor development at 2 years of age [5]. The results of this study [5] showed that the worse obstetric outcome might be much more influenced by genital tract infection, not by urinary tract infection. All findings question a

routine screen-treat-policy for asymptomatic bacteriuria in pregnancy.

A recent Cochrane review concluded that antibiotic treatment is effective in reducing the risk of pyelonephritis, low-birth-weight newborns, and preterm birth in pregnancy; however, the authors also emphasized that the effect of antibiotic treatment is very much uncertain because of the very poor quality of the included studies and the very low quality of the evidence [6]. That is why a recent systematic review and meta-analysis concluded that to date, no reliable evidence supports routine screening for asymptomatic bacteriuria in pregnant women [7].

The benefits and harms of antibiotic use for women with asymptomatic bacteriuria, regardless of pregnancy or not, are always discussed [8–10]. A Cochrane Review of 9 clinical trials examining treatment of asymptomatic bacteriuria concluded that treatment does not always decrease the frequency of symptomatic infection; by contrast, significantly increases the number of adverse events and sometimes may actually increase the risk of future symptomatic urinary tract infections [10]. Therefore, it is welcome that research studies have focused on more accurate clinical and microbiologic surveillance systems, validated risk stratification strategies, better point-of-care testing, and identification of promising and appropriate antibiotic use, to offer a better intervention and management to prevent maternal and newborn deaths related to these infections [11]. Unfortunately, recent new information from cultivation-independent molecular-based techniques has demonstrated that the study of genitourinary infection is not a single entity because of the different sub-types with different etiologies, different microbial communities, different responses to antibiotics, and of greatest importance, different clinical outcomes. Such evidence clarifies why the microbiology of genitourinary infection remains uncertain, and why the response to antibiotics remains inconclusive [11]. Therefore, the other strategy might be considered, such as restoration of normal genitourinary tract microbiomes, including *Lactobacillus* supplementation [12,13], which might improve the obstetric outcomes [14,15]. Lai's study showed the strong association of pregnant women with asymptomatic bacteriuria and their adverse pregnancy outcomes [1] and this supported the clinical guide—the existing, widespread, long-standing practice of screening and treatment for bacteriuria in pregnant women. In fact, this standard approach has unquestionably improved pregnancy outcomes for many women [3].

In conclusion, there is much uncertain for the topic, which has been shown as a manuscript tile—"Do pregnant women with asymptomatic bacteriuria need treatment?". To respond to this question needs much more trials to test what is the better strategy in the diagnosis and management of pregnant women with asymptomatic bacteriuria.

### Conflicts of interest

The authors declare that they have no conflicts of interest related to the subject matter or materials discussed in this article.

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