

# Journal Pre-proof

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## **Does improved management of asymptomatic bacteriuria in pregnant women prevent E. coli bloodstream infections?**

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Dear Sir,

Untreated, asymptomatic bacteriuria (ASB) in pregnancy is reported to be associated with an increased risk of pyelonephritis. Preventing pyelonephritis might prevent bloodstream infections (BSI) with *Escherichia coli* (*E. coli*), which could contribute to the Department of Health 2017 initiative to reduce Gram-negative BSI in England by 50% by 2021[1]. The NICE Clinical Guideline Antenatal Care for Uncomplicated Pregnancies [2], recommends offering routine culture-based screening for ASB during early pregnancy. However, testing practices for ASB in England are variable between hospitals [3].

ASB screening was performed routinely at Birmingham Women's Hospital (BWH), but it was identified that many patients had missed or delayed treatment. In May 2015, we implemented a new compulsory multidisciplinary care pathway to ensure that all women with true ASB detected in their booking urine were treated promptly. True ASB was defined as the presence of  $>10^5$ /ml of an unequivocal uropathogen in one sample, or  $>10^5$ /ml of an equivocal uropathogen in two samples. If true ASB was detected a letter was sent to the patient and her General Practitioner to ensure that treatment was initiated promptly. Patients were then followed up regularly with repeat urine samples for culture for the rest of their pregnancies. We reviewed BSI with *E. coli* in maternity cases before and after implementation of the pathway, to determine whether this initiative has impacted the occurrence of BSI with *E. coli* in this population.

The Microbiology Department maintains a prospective database of all BSI at BWH, which includes details on the underlying focus of the infection. Overall, the number of cases that were urinary tract-related has remained relatively constant throughout the observation period (Figure 1). However, pre-intervention 3 of the 5 urinary tract infection (UTI) related BSI were in antenatal women whereas, all of the 5 UTI-related BSI post-intervention were postnatal. The increase in overall numbers of cases of *E. coli* BSI in 2016-17 is difficult to explain. We hypothesise that the increase may have reflected an increased detection of BSI because of the success of sepsis awareness programmes such as the RCOG Green-top Guideline Bacterial Sepsis in Pregnancy. In support of this, the number of blood cultures (BC) received from maternity cases almost doubled from 349 in 2014-15 to 689 in 2018-19.

A Welsh study also reported an increase in BC taken due to sepsis awareness, which correlated with an increase in *E. coli* detection [4]. The subsequent decrease in numbers of *E. coli* BSI may be because further improvement in sepsis awareness is leading to better recognition and treatment of early signs of infection thereby avoiding BSI.

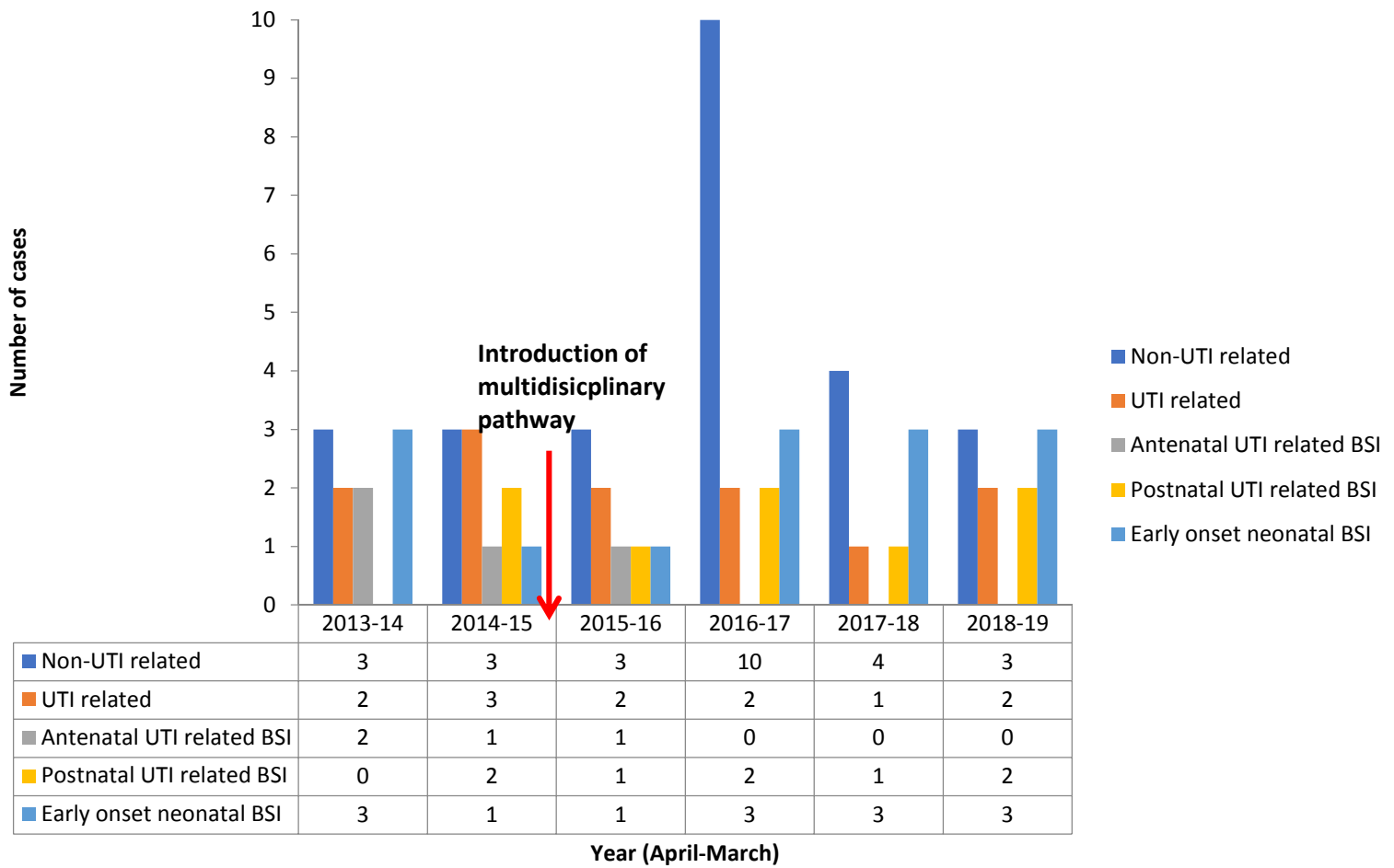
Analysis also indicated the number of early onset neonatal *E. coli* BSI has remained constant from year to year (Figure.1), suggesting that the introduction of a multidisciplinary ASB pathway did not impact the prevalence of early onset neonatal BSI, despite the reduction in antenatal UTI BSI in pregnant women.

Universal screening for ASB in pregnancy has been the subject of controversy. Our study suggests that a multidisciplinary pathway is effective in preventing antenatal UTI related *E. coli* BSI. A recent systematic review reported that antibiotic treatment for pregnant women with ASB likely reduced the incidence of pyelonephritis, but the magnitude of the effect was uncertain. This study also reviewed screening multiple times over one-time screening, finding no significant evidence [5]. A previous Cochrane review concluded that routine screening was associated with a reduction in the incidence of pyelonephritis from 3-4% to 0.5% [6]; however, the evidence was assessed as low quality. The UK NSC continues to recommend that there is insufficient information to recommend a population screening programme [7], which was corroborated by a 2016 systematic review [8].

We do not know whether a systematic approach to ASB management has had any other positive or negative effects (e.g. less or more antibiotic administration, or avoidance of pyelonephritis without bacteraemia). However, it does not appear to be associated with reduction of *E. coli* BSI. This study is limited by the small sample size. Also, we have not formally assessed compliance with the protocol; however, because a midwife has allocated time to oversee the follow-up of women with ASB we believe that compliance is good. Large trials are required to determine the clinical and cost effectiveness of screening before the results can be generalised, and to definitively address the dichotomy between NSC and NICE guidance.

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**Figure 1. Numbers of cases of *E. coli* Bloodstream infections (BSI) in pregnant women and of early onset neonatal BSI, by year.**