Risk of Urinary Tract Infection Among Pregnant Women with Anemia: A Systematic Review and Meta-Analysis

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Abstract

Objective: This study aims to provide an evidence-based answer to whether anemia during pregnancy is a risk factor for the development of urinary tract infections (UTIs).

Methods: The method used in this study was a systematic review and meta-analysis conducted in accordance with the PRISMA guidelines. A literature search was performed in PubMed, ScienceDirect, and Scopus databases for observational studies reporting the occurrence of anemia during pregnancy and UTIs. Quantitative synthesis of pooled odds ratios (ORs) with 95% confidence intervals (CIs) was conducted using Review Manager 5.4 software and visualized through forest plot graphs.

Result: Based on nine articles included in the analysis, anemia during pregnancy was found to be significantly associated with the occurrence of UTIs [Pooled OR 2.38, 95% CI: 1.24–4.56; $p < 0.00001$], but not with asymptomatic bacteriuria (ASB) [Pooled OR 2.08, 95% CI: 0.89–4.90; $p = 0.09$]. When both outcomes were combined as total bacteriuria, the analysis demonstrated a statistically significant association [Pooled OR 2.27, 95% CI: 1.38–3.75; $p < 0.0001$].

Discussion: Anemia during pregnancy increased the risk of UTIs by 2.38 times higher than without anemia, which occurs through the mechanism of immune system dysregulation. Monitoring hemoglobin levels in the antenatal period can be an effort to screen for risk factors for UTIs.

Conclusion: Anemia during pregnancy is a risk factor for the development of UTIs and bacteriuria, but not a risk factor for ASB. Early evaluation of risk factors and management of anemia are important efforts for clinicians to prevent the development of UTIs during pregnancy.

Keywords: Anemia; risk factors; urinary tract infection; pregnancy; meta-analysis

Risiko Infeksi Saluran Kemih pada Ibu Hamil dengan Anemia: Tinjauan Sistematis dan Meta-Analisis

Abstrak

Tujuan: Penelitian ini bertujuan untuk memberikan jawaban berbasis bukti mengenai apakah anemia selama kehamilan merupakan faktor risiko untuk perkembangan ISK atau bukan

Metode: Metode yang digunakan dalam penelitian ini adalah tinjauan sistematis dan meta-analisis yang disusun berdasarkan PRISMA guideline. Pencarian literatur dilakukan melalui basis data PubMed, ScienceDirect, dan Scopus pada penelitian observasional yang melaporkan kejadian anemia selama kehamilan dan infeksi saluran kemih (ISK). Analisis kuantitatif untuk gabungan *odd ratio* dengan interval kepercayaan 95% dilakukan menggunakan perangkat lunak Review Manager 5.4 dan divisualisasikan dengan grafik *forest plot*

Hasil: Berdasarkan 9 artikel yang disertakan dalam analisis menunjukkan bahwa anemia selama kehamilan memiliki hubungan yang signifikan terhadap kejadian ISK [Pooled OR 2.38, 95% CI: 1.24—4.56; $p<0.00001$], tetapi tidak untuk bakteriuria asimtomatik (ASB) [Pooled OR 2,08, 95% CI: 0,89—4,90; $p=0,09$]. Kami menggabungkan kedua hasil untuk total bakteriuria dan menunjukkan signifikansi statistik [Pooled OR 2,27, 95% CI: 1,38—3,75; $p<0,0001$].

Pembahasan: Anemia selama kehamilan dapat meningkatkan risiko ISK sebesar 2,38 kali lebih tinggi daripada tanpa anemia yang terjadi melalui mekanisme disregulasi sistem imun. Pemantauan kadar hemoglobin pada periode antenatal dapat menjadi upaya skrining faktor risiko terjadinya ISK.

Kesimpulan: Anemia selama kehamilan merupakan faktor risiko untuk perkembangan ISK dan bakteriuria, tetapi bukan faktor risiko untuk ASB. Evaluasi faktor risiko dan penatalaksanaan anemia lebih dini menjadi upaya penting bagi klinisi dalam mencegah perkembangan terjadinya ISK selama kehamilan

Kata kunci: Anemia; faktor risiko; infeksi saluran kemih; kehamilan; meta-analisis

Introduction

Urinary tract infections (UTIs) are the most common bacterial infections during pregnancy which clustered in a spectrum from asymptomatic bacteriuria (ASB) and symptomatic bacteriuria including cystitis and pyelonephritis.[1] A systematic review and meta-analysis of the global prevalence of UTI in pregnant women which included a total of 30,641 participants reported the prevalence was 23.9%.[2] The issue of antimicrobial resistance might be the reason why the prevalence of these infections is higher in developing countries than in developed countries. The study conducted in a developing country, Indonesia, reported the prevalence of ASB is 10.5% from the 715 pregnant women with the most common etiology being *Escherichia coli* (26.7%), followed by *Klebsiella pneumonia* (20%), and *Streptococcus agalactiae* (9.3%).[3,4] The presence of UTI during pregnancy, especially an untreated UTI was associated with maternal and fetal complications, including chorioamnionitis, preterm delivery, intrauterine growth restriction, and low birth weight. These infections are also reported as contributing factors for the offspring's susceptibility to neonatal and pediatric infections, including otorhinolaryngological and respiratory infections.[5] Therefore, understanding the management to reduce morbidity and analyzing the risk factors to prevent being are important factors. Many published studies reported the important risk factors associated with UTI, such as personal hygiene, history of diabetes mellitus, history of UTI, and anemia during pregnancy.[6,7] Physiological changes due to high metabolic demands might lead to the presence of anemia during pregnancy. The multi-center cohort study from 2016 to 2020 reported that the high prevalence of anemia at any stage during pregnancy was 34.59%.[8] There are many associated factors with anemia in pregnant women including gestational age in the third trimester, lack of antenatal care visits, and absence of iron supplementation.[9] Although the current published studies demonstrated that anemia during pregnancy increased the risk of developing UTI. However, the robustness of the evidence remains unclear due to the variety of populations, and most was conducted in a single-center area. Thus, we conducted a systematic review and meta-analysis of observational studies to investigate if the risk of UTI is increased in pregnant women patients with anemia compared with non-anemia pregnant women participants.

Methods

Literature search

We conducted a systematic review and meta-analysis according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA guideline.[10] This study was registered on PROSPERO (CRD420251130349).

Literature search

The electronic databases for the literature search were performed in *Scopus*, *ScienceDirect*, and *PubMed* till January 25, 2025, using the formulating keywords: "Anemia", "Risk factors", "Urinary Tract Infection", and "Pregnancy". We restricted the language to English only. All results from the electronic databases were imported to Rayyan.ai for selection.[11]and no single method fulfills the principal requirements of speed with accuracy. Automation of systematic reviews is driven by a necessity to expedite the availability of current best evidence for policy and clinical decision-making. We developed Rayyan (http://rayyan.qcri.org

Eligibility Criteria

The eligibility criteria for the included studies

were (1) observational study comparing the risk of UTI between pregnant women with and without anemia, (2) reporting the UTI spectrum for symptomatic or asymptomatic bacteriuria, (3) providing the outcomes parameters for the events per population, odds ratio (OR), or sufficient raw data to calculate these ratios. The exclusion criteria were (1) duplicate study, (2) irrelevant topic, (3) irretrievable full-text article, (4) study with incomplete data, (6) review article, conference abstracts, and letter to the editor, (7) non-human studies. Two independent investigators (MFW and RNE) assessed the collected articles based on title and abstract screening and then full-text review according to the eligibility criteria. Consensus with all authors will be realized if the discrepancies between investigators are observed.

Data Extraction

Data extraction of all included studies was performed by two investigators (MFW and RNE) independently. The information was extracted including the first author's last name, year of publication, country, study design and time period, patient characteristics, population, bacterial culture, and important findings for the association of anemia and UTI. Any discrepancies were resolved by consensus with all authors

Statistical Analysis

The quantitative analysis for the included studies was performed using Review Manager (RevMan) 5.4 software from the Cochrane Collaboration (London, United Kingdom). The pooled data for odds ratio (OR) from each study were conducted using the generic inverse variance method of DerSimonian and Laird.[12] At the outcomes reported for events per total population rather than the OR, we estimated the OR from the events per total population using the RevMan calculator. Random effects or fixed-effect models were chosen based on the heterogeneity. If a high heterogeneity was observed ($I^2 \geq 50\%$), the random effect was used. The subgroup analyses were clustered for the explicit outcomes for UTI and specified for ASB. We also reported the combination of these outcomes for the risk of total bacteriuria

Result

We identified 1478 articles from the database search, and 9 articles were eligible for the analysis after undergoing the selection process (Figure 1). Based on the included studies, most study was conducted by a cross-sectional design with a total of 7 studies. The varied distribution of countries was reported including two studies in Ethiopia and one study in the USA, Thailand, Congo, Egypt, Saudi Arabia, India, and China. There are a variety of bacterial cultures, with the most commonly reported bacteria is *Escherichia coli*. The data extraction for the included studies is presented in Table 1.

The quantitative analysis (figure 2) showed anemia is statistically significant for urinary tract infections [Pooled OR 2.38, 95% CI: 1.24—4.56; $p<0.00001$] with high heterogeneity was observed ($I^2=92\%$). This result was not in line with the asymptomatic bacteriuria [Pooled OR 2.08, 95% CI: 0.89—4.90; $p=0.09$] that also reported high heterogeneity ($I^2=77\%$). The accumulation of both subgroups for the total bacteriuria demonstrated statistically significant [Pooled OR 2.27, 95% CI: 1.38—3.75; $p<0.0001$] with high heterogeneity was observed ($I^2=88\%$).

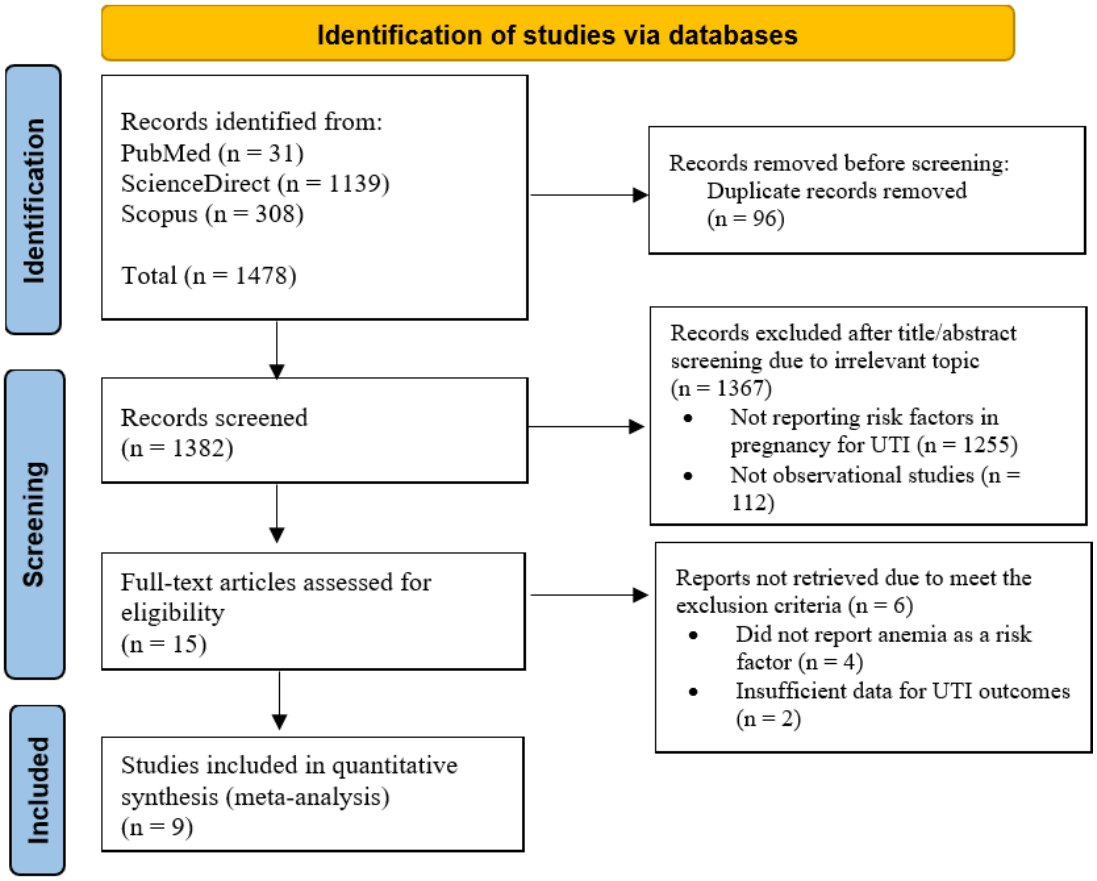

Figure 1. PRISMA Flow chart showing the study selection process

Table 1. Data extraction of included studies

First author	Study design; time period	Patients characteristics	Population	Bacterial culture	Results
Schieve et al., 1994[13] (USA)	Retrospective cohort, multi-center; 1983 – 1989	Pregnant women from 14 hospitals in the Chicago area	(+) culture: 1,988 (-) culture: 23,758	Not reported	Maternal anemia was a risk factor for UTI [Adjusted OR 1.6; 95% CI: 1.3—2]
Kovavisarach et al., 2009[14] (Thailand)	Cross-sectional, single-center; August 2005 – October 2005	Asymptomatic pregnant woman who attended their 1st antenatal appointent	(+) culture: 36 (-) culture: 324	*Lactobacillus species* (25%), *Escherichia coli* (22.2%), *Streptococcus viridans* (22.2%), *Gardnerella vaginalis* (13.8%), *Proteus mirabilis* (5.6%), *Staphylococcus saprophyticus* (5.6%), *Enterococcus feacalis* (2.8%), *Klebsiella pneumoniae* (2.8%)	Anemia was not statistically associated with ASB with the prevalence 11/36 in the (+) culture and 74/324 in the (-) culture [OR 1.436; p=0.345]
Emiru et al., 2013[15] (Ethiopia)	Cross-sectional, single-center, January 2011 – April 2011	Pregnant woman who attended the antenatal care clinic	(+) culture: 35 (-) culture: 332	Not reported	Anemia was a significant risk factor for UTI [OR 4.388; 95% CI: 1.776—10.839; p=0.003]
Tandu-Umba et al., 2015[16] (Congo)	Cross-sectional, single-center; March 2012 – August 2014	Singleton pregnancy was delivered at the maternity of the Department of Obstetrics & Gynecology	(+) culture: 62 (-) culture: 350	Not reported	Anemia was significantly linked to urinary infection [OR 1.6, 95% CI: 1.0—2.5; p=0.03]

Shaheen et al., 2016[6] (Egypt)	Nested case-control in a cross-sectional investigation, single center; September – November 2014	All pregnant women who attended the center for antenatal care	(+) culture: 79 (-) culture: 171	Not reported	Anemia was a significant risk factor for developing UTI with the prevalence 48/79 in the (+) culture and 47/171 in the (-) culture [OR 3.2, p<0.0001]
Ali et al., 2018[17] (Ethiopia)	Cross-sectional, single center; February – May 2017	All pregnant women who attended antenatal check-ups at the Referral Hospital without any signs and symptoms of UTI	(+) culture: 56 (-) culture: 302	*S. aureus* (30.35%), *E. coli* (30.35%), *CoNS* (26.80%), *Enterobacter aerogenes* (1.8%), *K. Pneumoniae* (3.6%), *S. agalactiae* (3.6%), *CoNS* and *S. aureus* (1.8%), *CoNS* and *E. coli* (1.8%)	Anemia was significantly associated with the prevalence of ASB [Adjusted OR 4.977, 95% CI: 2.4—10.3; p<0.0001]
Al-Kashif, 2020[18] (Saudi Arabia)	Cross-sectional, single-center; October 2018 – March 2019	Pregnant women at the 2nd trimester of pregnancy who attended the antenatal clinic with suspected clinical symptoms of UTI	(+) culture: 162 (-) culture: 141	*E. coli* (37%), *Klebsiella pneumonia* (27%), *Staphylococcus spp* (17.6%), *Proteus spp* (8.2%), *Klebsiella Oxytocia* (6.5%), *staphylococcus saprophytic* (3.7%)	Anemia was not statistically associated with UTI with the prevalence 57/162 in the (+) culture and 66/141 in the (-) culture [p=0.235]

Mishra et al., 2024[19] (India)	Cross-sectional, single-center; October 2023 – December 2023	Pregnant women who attended the antenatal appointments; had not taken antibiotics within two weeks prior to the sample collection; refrained from consuming a large volume of water within one hour before sample collection	(+) culture: 51 (-) culture: 243	*E. coli* (51%), *Klebsiella* (19%), *Enterococcus* (14%), *Staphylococcus* (12%), Others (4%)	Anemia was not statistically associated with ASB with the prevalence 15/51 in the (+) culture and 61/243 in the (-) culture [OR 1.24, 95% CI: 1.02—1.29; p<0.522]
Shen et al., 2024[7] (China)	Cross-sectional; single-center; October 2019 – October 2023	20 – 45 years pregnant women who attended the obstetric clinic of the study hospital for prenatal check-ups	(+) culture: 56 (-) culture: 544	*E. coli* (46.43%), *Staphylococcus aureus* (23.21%), *Streptococcus pneumonia* (8.93%), *Klebsiella genus* (8.93%), *Candida genus (7.14%), Proteobacteria* (5.36%),	Anemia was a significant risk factor for UTI Hb <100 g/L has an OR 8.022, 95% CI [OR 8.022, 95% CI: 4.532—14.325; p<0.001]

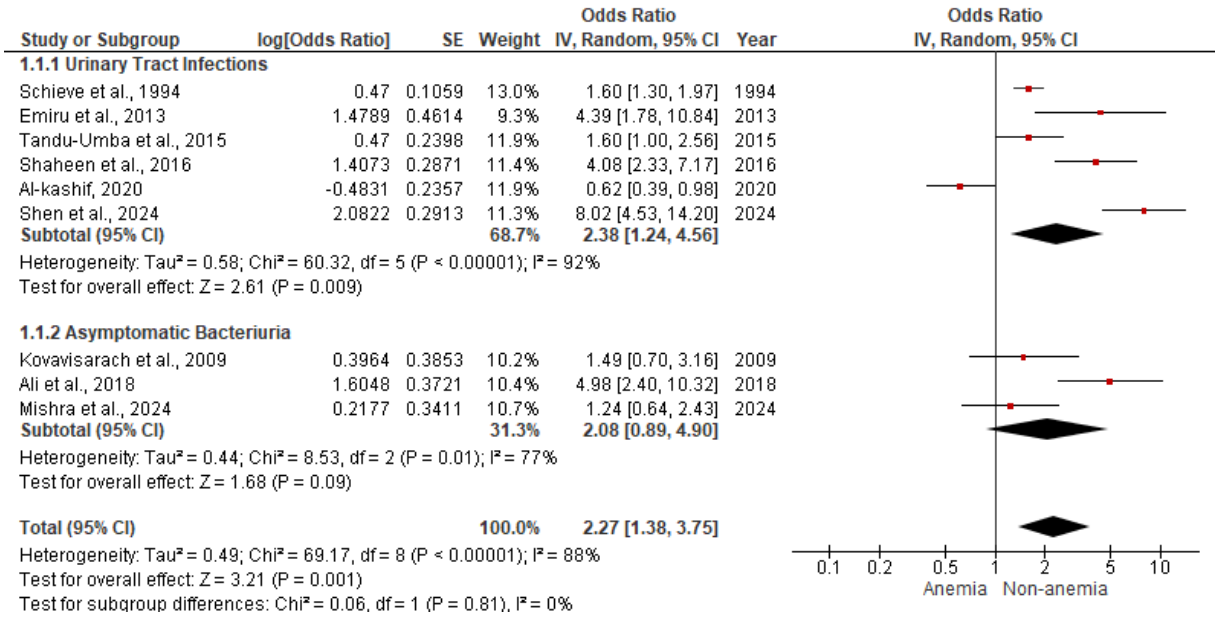

Figure 2 Forest plot of the risk of pregnant women with anemia for the developing of UTI

Discussion

As far as we know, this is the first systematic review and meta-analysis that systematically assessed all available data on the risk of UTI among pregnant patients with anemia. Statistical significance was observed for the development of UTI 2.38 times in pregnant women with anemia compared to pregnant women without anemia. The mechanism of why pregnant women with anemia have a higher risk of UTI remains unclear. However, the hypotheses might be explained as the dysregulation of immune systems due to iron deficiency, leading to a decrease of the production and function of antibodies, including neutrophils, macrophages, and lymphocytes so the body becomes less effective against the bacteria. This condition has resulted in more vulnerability to infections during pregnancy, such as respiratory infections, urinary tract infections, and other bacterial or viral infections. Furthermore, the exacerbation of the inflammatory response due to infections might increase the risk of pregnancy complications in both the maternal and neonatal.[20–22]

A retrospective case-control study involving 230 patients with upper UTI during pregnancy stated urosepsis could develop from UTI at the time when the identified risk factors were hydronephrosis during pregnancy or secondary to reno-ureteral lithiasis of at least 2nd grade, fever over 38 ◦C, and moderate anemia. During pregnancy, the plasma volume is distributed faster than the production of blood cells which leads to relative anemia. They showed anemia for the increased risk for urosepsis with OR 2.622, which provides a perspective on the presence during pregnancy, morbidity is not only focused on the new onset of infection, but also associated with the progression of a pre-existing infection to a more severe progression.[23]

This study reported that the most frequent bacterial culture in sepsis patients is *E. coli* (54.5%), followed by *Klebsiella spp.* (13.6%), and *Proteus mirabilis* (1.5%). These culture results are also in line with non-sepsis patients with a prevalence of 62.8%, 47%, and 6.1%.[23] In our two included studies, *E. coli* was also reported as the most frequent bacterial culture from urine isolates.[7,18] These

results indicate very similar trends in the prevalence of various causative organisms for UTI. We also analyzed the risk of ASB among pregnant women with anemia with a pooled OR was 2.08. Although the results showed no statistical significance, the higher trend of ASB in pregnant women with anemia means that the risk of ASB cannot be underestimated. This result required caution to interpret because the insignificant results for ASB might be due to the quantitative analysis only eligible for three included studies. Three included studies for the ASB showed that the most frequent culture was *E. coli*, reported by Mishra et al., 2024 for 51% and Ali et al., 2018 for 30.35%.[17,19] Kovavisarach et al. 2009 reported *E. coli* was the second most frequent with a prevalence of 22.2% after *Lactobacillus species* with a total of 25%.[14] The most common etiology of UTI is Gram-negative bacteria compared to Gram-positive bacteria. The specific structure of gram-negative bacteria might be an important factor that facilitates to invasion of the epithelial tissue, leading to infection during pregnancy. Among pregnant patients with UTI, general safety is an important consideration in prescribing antibiotics. Beta-lactam antibiotics, such as penicillins and cephalosporins can be prescribed as the antibiotic of choice to eradicate the etiology in pregnant women patients with UTI.[2] Furthermore, for the preventive strategies, monitoring hemoglobin levels during the antenatal period was an important effort in identifying the presence of anemia as a risk factor. This effort provides consideration for early intervention before complications occur.

The strength of this study was conducted by a systematic review and meta-analysis approach that allows a comprehensive estimation of the risk factor. Providing a piece of robust evidence to recognize the association between anemia during pregnancy and UTI. However, although many included studies stated that anemia is a risk factor, these studies were mostly conducted cross-sectional design. It led to the identification being clearly for the association rather than establishing the causality.

Conclusion

Anemia during pregnancy is a risk factor for the development of UTI and bacteriuria, but not for ASB. Early evaluation of risk factors and management of anemia are important efforts for clinicians to prevent the development of UTI during pregnancy.

Conflict of Interest

The authors declared that there is no conflict of interest in this study.

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