Factors Affecting Clinical Outcomes of Neonates Born to Mothers with Urinary Tract Infection in a Tertiary Private Hospital

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ABSTRACT

Background: Urinary tract infections (UTIs) during pregnancy pose significant risks to both maternal and neonatal health. This study determined the association between maternal characteristics and neonatal clinical outcomes in mothers with UTIs.

Methods: A retrospective analysis was conducted on 151 mothers diagnosed with UTIs during pregnancy. Data from 2021 to 2024 were collected from medical records of a tertiary private hospital, including maternal age, comorbidities, antibiotic use and neonatal outcomes such as preterm birth and clinical sepsis. Statistical analyses using Poisson regression identified significant predictors of adverse neonatal outcomes, reported as adjusted Prevalence Ratio (aPR) and 95% Confidence Interval (95% CI).

Results: Most mothers were aged 20-35 years (72.19%). The prevalence of preterm births among the neonates was 21.85%, while 41.06% exhibited clinical sepsis. Key findings indicated that younger maternal age (<19 years) significantly decreased the risk of preterm births (aPR: 0.20, 95% CI: 0.05–0.84). Maternal kidney disease was a strong predictor of preterm births (aPR 14.30, 95% CI: 3.91–52.24) and clinical sepsis (aPR 3.60, 95% CI: 2.02–6.41) in neonates. Maternal autoimmune disease also emerged as a significant predictor, with an increased risk of clinical sepsis (aPR 3.05, 95% CI: 1.81–5.11). Lastly, antibiotic use, particularly ampicillin, was associated with a higher risk of preterm births (aPR 3.26, 95% CI: 1.31–8.07), reflecting the severity of underlying infections.

Conclusion: The study highlights the critical role of maternal age and comorbidities, such as kidney disease, in influencing neonatal outcomes in pregnancies complicated by UTIs. Younger maternal age and kidney disease significantly increase the risks of preterm births and clinical sepsis. Enhanced prenatal care protocols and targeted interventions for high-risk groups are essential to improve maternal and neonatal health outcomes.

Key words: neonates, urinary tract infection, kidney disease

During pregnancy, urinary tract infection (UTI) is a prevalent problem that results in maternal and neonatal complications both in developing and developed countries (Kalinderi, et al, 2018; Matuszkiewicz-Rowińska, et al, 2015). In fact, maternal UTI has been shown to be a risk factor for adverse outcomes on the child such as premature birth and/or low birth weight, neonatal sepsis, and even death (Alam, et al, 2014; Rafi, et al, 2020). The overall global prevalence of maternal UTI is around 22% to 35%, and especially higher in third world countries (Vogel, et al, 2014). There are different underlying factors that make pregnant women at risk for developing UTI such as anatomical, physiological and personal factors (John, et al, 2016). Some of these causes include increased maternal age, gravidity, frequency of intercourse, gestational diabetes, sickle cell anemia, history of previous urinary tract infection, immunocompromised state, and abnormalities in the genitourinary system (El-Kashif, 2019; Korb, et al, 2018; Vasudevan, 2014). Due to urethral dilatation and increased urine volume, this causes increased urinary retention in the bladder, and in turn, the

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reflux of the urine to the urethra causes an increase in the plasma volume, which ultimately reduces the concentration of the urine (Gillenwater, 1978). Another common instance, in about 70% of pregnant women, is the presence of reducing sugars in the urine, such as glucose, galactose, lactose, and fructose in the urine. This increases the excretion of estrogen and progesterone, which can result in changes in the vaginal flora, and increased colonization of bacteria (Lindholm, 1973; Teeguarden, et al, 2016). There are two classifications of urinary tract infection in pregnancy. First, and is also the most common, is asymptomatic bacteriuria, which involves the lower genitourinary tract (Schnarr & Smaill, 2008; Ullah, et al, 2007). The second is Acute Pyelonephritis, which involves the upper part of the urinary tract (Loh & Sivalingam, 2007).

According to the World Health Organization, there are roughly annual five million newborn fatalities, 98% of which take place in developing countries (Ejerssa, et al, 2021; Sampaio, et al, 2018). The number of children worldwide who died from sepsis or infection has nearly increased over the previous 20 years (Riley & Wheeler, 2012). This may be as a result of the reality that most underdeveloped countries lack access to antibiotics primarily empirical because there are not many suitable laboratories. In many healthcare facilities, there are facilities for bacteria culture and sensitivity testing (Terblanche, et al, 2007). Furthermore, central nervous system (CNS) involvement, septic shock, or hypoxemia brought on by severe parenchymal lung disease can result in serious neurological sequelae in surviving neonates (Newman, et al, 2006). Therefore, the need to elucidate the significant factors affecting the clinical outcomes from neonates is more important than ever, in order to prevent unwanted mortality. Banking from this gap, this study will focus on the determination of the significant factors affecting the clinical outcomes of neonates born to mothers with UTI in a private tertiary hospital.

REVIEW OF RELATED LITERATURE

Maternal Infections

Infection during pregnancy imposes a direct impact on the growing fetus, and in some cases may even result to fetal death (Ornoy & Tenenbaum, 2006). These infections can occur at any stage of the pregnancy. TORCH infection (toxoplasmosis, rubella, cytomegalovirus, herpes, and others), syphilis, varicella zoster, and parvovirus B19 have been known to cause congenital malformations, intrauterine growth restrictions, and even abortion. Other common infections during pregnancy are Listeria monocytogenes, Chlamydia trachomatis, Neisseria gonorrhea, Group B Steptococcus, E. coli, Gardnerella vaginalis, Trichomonas vaginalis, Ureaplasma urealyticum, SARS-CoV2 MERS, Influenza, Plasmodium sp., and Candida sp (Buka, et al, 2001; Dauby, et al, 2012). These bacterial, viral, parasitic, and fungal pathogens can cross the placental barrier, and cause pregnancy complications such as vertical transmission, congenital diseases, abortion, preterm birth, low birth weight, and intrauterine growth restriction (Al-Adnani & Sebire, 2007; Kumar, et al, 2022; Pradhan, et al, 2023).

Maternal UTI

After anemia, urinary tract infection is the second most common complication in pregnancy, and if not recognized and treated early, can cause adverse outcomes to the infant and mother, including preterm birth, neonatal sepsis, low birth weight, and even neonatal and maternal mortality (Gilbert, et al, 2013). Anatomical and physiological changes that occur during pregnancy predispose them to this type of infection and its complications (Allen, 2021; Loh & Sivalingam, 2007). According to a study in Ethiopia, compared to neonates born to mothers who were clear from any urinary tract infection, neonates born to mothers with urinary tract infection had a 3.55 times higher risk for developing neonatal sepsis (Seyoum, et al, 2023).

Urinary tract infection during pregnancy will increase inflammatory reactions in maternal and fetal tissues, a mechanism that is directly associated with increased maternal and neonatal adverse outcomes, including preterm birth (Bolton, et al, 2012; Redman, et al, 1999). Roughly half of spontaneous preterm births are associated with intrauterine infections, which triggers maternal and fetal inflammatory responses, causing preterm birth by enhancing stimulation of uterine contractions. Moreover, in very preterm neonates, antenatal urinary tract infection predisposes them to systemic inflammation (Goldenberg, et al, 2000; Muglia & Katz, 2010).

In a local study at a tertiary hospital, the prevalence of urinary tract infection in pregnant women was 15.6% with the most common pathogen

isolated being Escherichia coli and Staphylococcus. In relation to age of gestation, comparison of the prevalence of urinary tract infection among the three groups shows that UTI occurred most frequent during the second trimester (Belete & Saravanan, 2020). Previous studies revealed that there was increased incidence of urinary tract infection starting on the sixth week of gestation, and peaks at the 22nd to 24th age of gestation (Alemu, et al, 2012; Sharma & Thapa, 2007; Sibi, et al, 2014). There is also increasing trend of probability of urinary tract infection for each pregnancy. Anatomical and physiological changes in pregnancy make them more susceptible to genitourinary tract infections, and may lead to pyelonephritis (Geerlings, 2016; John, et al, 2016). Some of the main reasons for this are expansion and distention of the bladder, and dilatation of the ureter (Laari, et al, 2022).

Clinical Outcomes of Neonates from UTI-infected Mothers

Neonatal sepsis can be categorized based on when it first manifests. Early Onset Sepsis (EOS) is defined as occurring within 0–7 days, whereas Late-Onset (LOS) for sepsis is 8–28 days (Haque, 2007). The distinction has clinical relevance, as EOS disease is mainly due to bacteria acquired before and during delivery, and LOS disease to bacteria acquired after delivery (nosocomial or community sources). Some publications make distinctions comparing very early onset sepsis (within 24 hours), early onset sepsis (EOS) (24 hours to sepsis (lasting longer than seven days) and LOS sepsis (Woldu, et al, 2014). In various institutions with various configurations, newborn sepsis has variable clinical outcomes. Early diagnosis and treatment are required to save the life of our future generation. Finding the common risk factors, the antibiotic usage pattern, and the clinical outcomes of newborn sepsis may require knowledge (Haque, et al, 1990; Haque, 2007).

Unfavorable health effects from UTI during pregnancy affect both the mother and the unborn child. In fact, antepartum UTI has been linked to perinatal outcomes that are unfavorable, including preterm birth, low birth weight, and even perinatal death (McGrady, et al, 1985). With an incidence ranging from 0.1% to 1% in term infants and between 4% and 25% in infants with very low birth weight, UTI in neonates is a common problem (Kaufman & Fairchild, 2004). Although some newborns may remain asymptomatic, in the majority of cases, the development of a UTI can lead to serious sickness states such growth failure, severe gastrointestinal symptoms, fever, irritability, lethargy, and jaundice (Piantino, et al, 2013). A thorough sepsis work-up for associated cases may also be necessary in some circumstances. Recent research suggests that maternal UTI followed by untreated neonatal UTI is a significant postpartum life-threatening occurrence. A substantial correlation between maternal and neonatal UTI was discovered in a recent study by Emamghorashi, et al. (2012) among Iranian newborns, and it was determined that 30.0% of neonates with UTIs and 6.8% of those without had mothers with a history of UTI (Emamghorashi, et al, 2012).

The importance of intra-partum is acknowledged in numerous research works. Pregnant women are more likely to experience fever and prenatal UTIs, which increase the likelihood that their unborn child will develop clinical early onset neonatal sepsis (EONS) (Etafa, et al, 2022). This is true because EONS is linked to the mother's microbial transmission during pregnancy and birth. For instance, in the United States, there is a 0.24% chance that an infant born to a woman who had an intrapartum fever may have neonatal sepsis. After the chorio-amnionic layers of the amniotic fluid rupture, the neonate typically experiences first colonization. The microbiota of the birth canal typically colonizes the child during delivery (Alexander, et al, 1999; Towers, et al, 2017).

Aspiration of contaminated amniotic fluid can cause fetal infection, which can end in stillbirth, preterm labor, or neonatal sepsis (Hutton & Thorpe, 2014). In addition, pregnant women with urinary tract infections are more likely to deliver premature or low birth weight babies, which increases the risk of neonatal sepsis. A source of Gram-negative septicemia and an increase in newborn mortality are both possible effects of urinary tract infections during pregnancy (Emiru, et al, 2013). Additionally, studies conducted in Saudi Arabia, Iran, Iraq, Malaysia, Uganda, and Israel found that changes in the physiologic-anatomy of the urinary tract and immune system during pregnancy raise the prevalence of urinary tract infections, which in turn causes unfavorable neonatal outcomes like bacteremia, toxic septicaemia, stillbirths, neonatal deaths, premature delivery, and low birth weight. In order to detect and treat urinary tract infections during pregnancy early and prevent the aforementioned consequences, screening pregnant women is crucial (Al-Mamoryi & Al-Salman, 2019;

Delzell Jr & Lefevre, 2000; Nteziyaremye, et al, 2020).

The objective of the study was to assess the clinical outcomes of neonates born to mothers with UTI and the maternal factors that affected them.

SIGNIFICANCE OF THE STUDY

Considering the importance of UTI in pregnant women which is responsible for several complications, its diagnosis and treatment are essential to maintain the health of mother and baby. This study will be able to identify significant factors contributing to unwanted neonatal mortality and morbidity from mothers with UTI. Evidence from this study may be utilized to guide the development of guidelines for preventing neonatal sepsis attributable to antenatal urinary tract infection thereby enabling to optimize neonatal survival in our institution.

Conceptual Framework of the Study

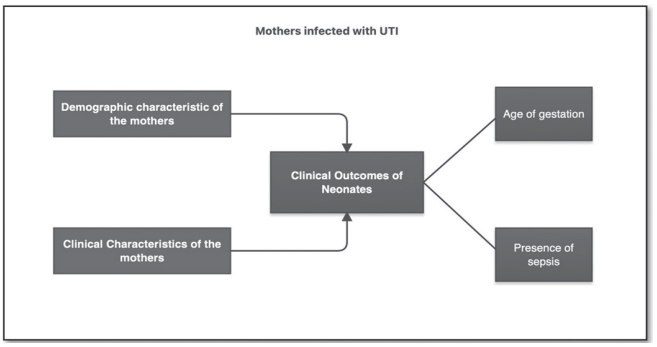

Figure 1. Conceptual framework of the study.

MATERIALS AND METHODS

Study Design and Setting

This is an observational, retrospective cross-sectional, and analytical study of neonates. The study was conducted at the Department of Child Health – Far Eastern University – Dr. Nicanor Reyes Medical Foundation Medical Center (FEU-NRMFMC).

A review of medical charts was done to collect information that included the patients' (mother and neonates) socio-demographics as well as their clinical profiles. Demographic data from all mothers with UTI based on a positive urine culture or urinalysis between January 2021 and April 2024 at FEU-NRMFMC were included in this study. In addition, medical records of all UTI-infected mothers diagnosed upon admission and who had given birth at FEU-NRMFMC were reviewed retrospectively for clinical and other pertinent data. Data extraction of medical records was carried out following the Case Report Form developed through Google Forms. Encoder was ensured to have sufficient expertise, particularly in handling medical records. A small subsample of at least 10% of the total records was reassessed to validate the data encoded into the developed database to identify inaccuracies and discrepancies during the encoding.

Study Population, Sample Size Calculation, and Sampling Procedure

Admitted pregnant patients and their neonates from 2021 to 2024 constituted the study population at FEU-NRMFMC. Over this period, a total of 151 patients were screened and recorded. This study aimed to include all eligible participants, ensuring comprehensive data collection and analysis.

The inclusion criteria for this study were specific and well-defined. Neonates born to mothers diagnosed with a urinary tract infection (UTI) based on urinalysis and urine culture were included. These mothers needed to have complete medical charts available for review to ensure the accuracy and reliability of the data collected. By focusing on neonates born to mothers with confirmed UTIs, the study sought to understand better the impact of maternal UTIs on neonatal outcomes.

Patients with incomplete medical charts were excluded from the study. This exclusion criterion was critical in maintaining the integrity of the data and ensuring that the findings were based on comprehensive and accurate medical records. The decision to exclude participants with incomplete medical charts was made to avoid potential biases and ensure that the study's conclusions were grounded in robust and complete data.

The total population of admitted pregnant patients and their neonates during the specified period was screened comprehensively, resulting in 151 eligible patients being included in the analysis. This thorough screening ensured that all potential participants were considered, and those meeting the inclusion criteria were included in the study. By screening the entire population, the study aimed to provide a comprehensive overview and ensure that the findings were representative of the broader population of pregnant patients and their neonates at FEU-NRMFMC during the study period. This approach

helped to enhance the study's validity and reliability, providing valuable insights into the relationship between maternal UTIs and neonatal health outcomes.

Data Collection

A Department of Child Health database was reviewed to identify infants delivered from 2021 to 2024 from mothers with UTIs. The list was counterchecked by reviewing the specimens sent to the Division of Pathology during the same period to ensure the inclusion of eligible patients. Once a list of patients was identified, medical records were retrieved by the primary investigator. Individual medical records were reviewed, and screening for inclusion criteria was performed to identify eligibility for inclusion in the study. Once deemed eligible, data collection was done using a standardized anonymized data collection form. Since the review of medical records was done and there was no direct patient interaction, obtaining informed consent was waived.

Once eligibility for inclusion in the study was ascertained, standardized data collection forms were used to collect data that was used in the subsequent analysis. The data collection tool utilized in the study was a Case Report Form, where all the data from the initial consultations and follow-ups were encoded. Data collection was accomplished by the primary investigator. Each patient was assigned to specific patient code assignments secured in a password-protected Excel file. Only the patient code and no identifier appeared on the data collection to ensure confidentiality. These forms were placed in a secure cabinet with a lock and stored in a private room. Data was tabulated using a password-protected Excel file on the primary investigator's laptop. The files' passwords were known only to the primary investigator. Patient records and data were only accessible to the study investigator.

For the variables collected, the demographic profile of the mothers, the clinical profiles of both mothers and neonates, and the clinical outcome of the neonates were included. The demographic and clinical profiles of the mothers included were: maternal age (in years), parity (1, 2 to 4, or >5), gravidity (1, 2 to 4, or >5), presence of comorbidities (no or yes), type of delivery (normal or Caesarian), types of antibiotics used, and the type of the most dominant microorganism. For the clinical profile of the neonates, the following were collected: sex (male or female), Apgar score, birthweight (not low birthweight ≥2500g; low birthweight <2500g), and weight appropriateness for age (>10th percentile for gestational age based on Lubchenco chart; <10th percentile for gestational age based on Lubchenco chart or small for gestational age). Lastly, the outcomes of the neonates were determined, including age of gestation (not preterm ≥37 weeks; preterm <37 weeks) and presence of sepsis (none or yes). Sepsis was considered when there was the presence of symptoms (poor suck, pathologic jaundice, respiratory distress, poor suck, fair activity, temperature instability, or apnea), complete blood count with platelet count was abnormal (thrombocytopenia, leukopenia, or leukocytosis), or blood culture was positive.

Data Analysis

Descriptive statistics was done to analyze the characteristics of the patients. Mean and standard deviation were used and compared for normally distributed data using two-sample t-tests. Categorical data was summarized as frequencies and percentages and were compared using either the Chi-square test or Fisher's exact test, as appropriate.

In terms of analyzing the primary outcome of the study, significant differences were assessed using Fisher's exact test due to the categorical nature of the data. Two sample t-tests for normally distributed variables and a Wilcoxon rank-sum test for non-normally distributed variables were also performed.

Associations between maternal factors and the neonatal outcome were estimated using linear models, a standard approach for analyzing cross-sectional studies. Associations between every ascertained covariate and the outcomes were estimated using bivariable generalized linear models (GLMs) with a Poisson distribution, log link function, and a robust variance; a suitable method for cross-sectional data with a common outcome (Spiegelman & Hertzmark, 2005; Tamhane, et al, 2016; Zou, 2004). Variables that were clinically relevant and a dummy variable for the various exposure were included in the model. In all models, all the other variables or covariates were controlled. These covariates were chosen a priori as potentially important predictors of the health outcomes. Furthermore, sensitivity analysis examined the influence of unmeasured confounding and expressed as E-values (Mathur, et al, 2018; VanderWeele & Ding, 2017). STATA 17 was used for all analyses and a p-value of less than 0.05 (or the

95% Confidence Interval) was considered significant for all the tests.

Ethical Considerations

Any form of patient information was processed with strict confidentiality following the Philippine Data Privacy Act of 2012. The investigator is Good Clinical Practice (GCP)-certified. Ethical clearance was sought from the FEU-NRMF Institutional Board. The study abided by the Principles of the Declaration of Helsinki (2013). It was conducted along with the Guidelines of the International Conference on Harmonization-Good Clinical Practice (ICH-GCP), E6 (R2), and other ICH-GCP 6 (as amended); National Ethical Guidelines for Health and Health-Related Research (NEGHHRR) of 2017.

Since the study design is a retrospective cross-sectional study that utilizes review of medical charts that poses no harm or benefit to patients included in the study, informed consent was waived for this study. Any form of patient identification did not appear in any data collection form, hence data privacy and confidentiality were maintained.

Patients were assigned numerical codes. The patient's age, sex, and hospital case number were the only identifiable personal information collected by the primary investigator. The data of patients with the corresponding patient code were stored in a password-protected Excel file and a password-protected laptop. Passwords were known only to the primary investigator as the designated information controller. Data collection forms and other patient information were kept in a cabinet with a security lock feature. They were stored safely and will only be processed within the hospital's premises. The data will be stored within 5 years in the said cabinet with a security lock under the custody of the information controller. After the said years, the primary investigator will shred the forms. Only the research investigator had access to the data collection forms. In accordance to the Data Privacy Act of 2012, the data protection officer of the institution will be accountable for compliance with applicable laws and regulations of the Act. In case of a breach of personal information during data collection, the incident will be reported to the data protection officer, who will then report it to the National Privacy Commission.

No risk occurred to the participants since no direct intervention was applied. Although the study did not directly benefit the patients included, its results can improve current management standards, which can eventually impact the outcomes of future patients.

The investigator had no conflicts of interest. The primary investigators shouldered the funding for the research study. The terms of Reference of the Collaborative Study and study-related insurance are not applicable in this study. The investigator started and financed this study. Due to the retrospective review design of the study, which predominantly involved reviewing medical charts, no compensation was given to the included patients.

RESULTS

Valid medical records that passed the screening procedure were included in the final analysis. Table 1 presents the demographic and clinical characteristics of mothers with UTI, encompassing a sample size of 151 individuals. The maternal age distribution indicated that the majority (72.19%) were between 20-35 years old, with a smaller proportion (27.15%) over 36 years old and only one individual (0.66%) under 20. Regarding comorbidities, 27.81% had diabetes, 19.21% had hypertension, 15.89% experienced premature rupture of membranes (PROM), and very few had autoimmune (1.32%) or kidney disease (1.32%). Regarding obstetric history, gravidity varied, with 37.75% having one pregnancy, 57.62% having 2-4 pregnancies, and 4.64% having more than five. Parity distribution was similar, with the majority having 1-4 previous births. Cesarean delivery was more common (60.26%) than vaginal delivery (39.74%).

Antibiotic usage varied, with high utilization of Cefuroxime (82.78%) and lower usage of other antibiotics like Amoxicillin and Cephalexin. The only pathogen identified was Escherichia coli, although it was detected in only one case (0.66%), with most tests not done (90.07%). Other pathogens, such as Staphylococcus aureus and Streptococcus viridans, were not tested or detected. Lastly, the "Other bacteria" refers to pathogens other than the commonly tested ones (Escherichia coli, Staphylococcus aureus, Streptococcus viridans, etc.) identified in the samples. These bacteria were detected in a very small number of cases (1 out of 15), and in most instances (136 out of 151, which is 90.07%), the specific bacterial tests were not performed. This category captures the presence of any less frequently encountered or tested bacterial pathogens in the study population of mothers with UTIs.

This study also documented other comorbidities such as bronchial asthma, heart conditions (including rheumatic heart disease and mitral valve prolapse), Hepatitis B infection, COVID-19 infection, Protein C & S Deficiency, HELLP syndrome, Rubella infection, Hypothyroidism, and Endometriosis. However, limited data was observed among the patients.

Table 1. Demographic and clinical characteristics of the mothers with UTI (n=151).

Characteristics	n (%)
Maternal Age, years	
≤19 years old	1 (0.66%)
20-35 years old	109 (72.19%)
≥ 36 years old	41 (27.15%)
Comorbidities	
Diabetes	
No	109 (72.19%)
Yes	42 (27.81%)
Hypertension	
No	122 (80.79%)
Yes	29 (19.21%)
Premature rupture of membranes (PROM)	
No	127 (84.11%)
Yes	24 (15.89%)
Autoimmune Disease	
No	149 (98.68%)
Yes	2 (1.32%)
Kidney Disease	
No	149 (98.68%)
Yes	2 (1.32%)
Presence of other comorbidities	
No	122 (80.79%)
Yes	29 (19.21%)
Obstetrics History	
Gravidity	
1	57 (37.75%)
2-4	87 (57.62%)
>5	7 (4.64%)
Parity	
1	66 (43.71%)
2-4	83 (54.97%)
>5	2 (1.32%)
Mode of Delivery	
Vaginal	60 (39.74%)
Caesarian	91 (60.26%)
Antibiotic Intake	
Amoxicillin	
No	150 (99.34%)
Yes	1 (0.66%)

Table 1. Demographic and clinical characteristics of the mothers with UTI (n=151).

Characteristics	n (%)
Co-Amoxiclav	
No	120 (79.47%)
Yes	31 (20.53%)
Ampicillin	
No	125 (82.78%)
Yes	26 (17.22%)
Cephalexin	
No	150 (99.34%)
Yes	1 (0.66%)
Cefuroxime	
No	26 (17.22%)
Yes	125 (82.78%)
Cefixime	
No	150 (99.34%)
Yes	1 (0.66%)
Nitrofurantoin	
No	151 (100.00%)
Yes	0 (0.00%)
Metronidazole	
No	132 (87.42%)
Yes	19 (12.58%)
Cefazolin	
No	148 (98.01%)
Yes	3 (1.99%)
Other antibiotics	
No	146 (96.03%)
Yes	6 (3.97%)
Pathogen Isolated	
Escherichia coli	
No	14 (9.27%)
Yes	1 (0.66%)
Not done	136 (90.07%)
Staphylococcus aureus	
No	15 (9.93%)
Yes	0 (0.00%)
Not done	136 (90.07%)
Achromobacter	
No	15 (9.93%)
Yes	0 (0.00%)

Characteristics	n (%)
Not done	136 (90.07%)
Enterococcus	
No	15 (9.93%)
Yes	0 (0.00%)
Not done	136 (90.07%)
Streptococcus viridans	
No	15 (9.93%)
Yes	0 (0.00%)
Not done	136 (90.07%)
Other bacteria	
No	14 (9.27%)
Yes	1 (0.66%)
Not done	136 (90.07%)

Table 2 outlines the demographic and clinical characteristics of neonates born to mothers with UTI. The sex distribution showed that 55.63% were male and 44.37% were female. The Apgar scores at the first, fifth and tenth minutes comprehensively assessed the newborns' health. At the first minute, most neonates (95.36%) scored between 7 and 10, which was reassuring and indicated good neonatal outcome, while 4.64% had scores between 4 and 6, suggesting moderate distress. No neonates scored between 0 and 3, indicating severe distress at this time point. By the fifth minute, the condition of most neonates had improved, with 98.01% scoring between 7 and 10, reflecting good neonatal outcomes. Only 1.99% had scores between 4 and 6, and none scored between 0 and 3. This trend continued at the tenth minute, where all neonates assessed scored between 7 and 10, showing good neonatal outcomes. However, it is important to note that for the majority (98.01%), the tenth-minute Apgar score was not recorded, likely because their earlier scores indicated they were stable. Most neonates (74.83%) had appropriate birthweight, while 25.17% were classified as low birthweight (LBW).

Antibiotic intake among neonates varied, with ampicillin being administered to 29.80%, gentamicin to 41.06%, and amikacin to 31.13%. Other antibiotics like cefotaxime, meropenem, and vancomycin were used less frequently. The most dominant pathogens identified included Group B Streptococcus and Escherichia coli, though in ~28% cases, these tests were not done. Abnormal blood counts were observed in some neonates, with anemia at 9.27%, leukopenia at 1.99%, leukocytosis at 3.97%, and a high absolute neutrophil count at 41.06%. Culture-positive sepsis was found in 2.65% of the neonates.

Table 3 details the clinical outcomes of neonates born to mothers with UTI. The age of gestation showed that the majority of neonates (78.15%) were not preterm, having a gestational age of more than 37 weeks, while 21.85% were preterm, born before 37 weeks of gestation. Clinical sepsis was observed in 41.06% of the neonates, whereas 58.94% did not exhibit symptoms of sepsis.

Table 4 presents the association between maternal characteristics and clinical outcomes of neonates born to mothers with UTI, specifically focusing on the risks of having preterm neonates and clinical sepsis, measured at a 95% confidence interval (CI). Significant predictors for the risk of having preterm neonates included maternal age, kidney disease, mode of delivery, and antibiotic intake. Specifically, neonates born to mothers aged 20-35 years had a significantly lower risk (adjusted Prevalence Ratio [aPR] 0.20, 95% CI: 0.05–0.84) compared to those aged less than 19 years. In other words, this effect estimate suggests that the risk of having a preterm neonate is reduced by 80% for mothers aged 20-35 years relative to mothers aged less than 19 years. Kidney disease was also a strong predictor, with an aPR of 14.30 (95% CI: 3.91–52.24). This means that mothers with kidney disease were 14 times more at risk

Table 2. Demographic and clinical characteristics of the neonates born to mothers with UTI (n=151).

Characteristics	n (%)
Sex	
Male	84 (55.63%)
Female	67 (44.37%)
First Minute Apgar score	
0-3	0 (0.00%)
4-6	7 (4.64%)
7-10	144 (95.36%)
Fifth Minute Apgar score	
0-3	0 (0.00%)
4-6	3 (1.99%)
7-10	148 (98.01%)
Tenth Minute Apgar Score	
0-3	0 (0.00%)
4-6	0 (0.00%)
7-10	3 (1.99%)
Not applicable	148 (98.01%)
Birthweight	
Not LBW >2500g	113 (74.83%)
Low birthweight <2500g	38 (25.17%)
Weight for age percentile	
>10th percentile (AGA/LGA)	146 (96.69%)
<10th percentile (SGA)	5 (3.31%)
Antibiotic Intake	
Ampicillin	
No	45 (29.80%)
Yes	106 (70.20%)
Gentamicin	
No	89 (58.94%)
Yes	62 (41.06%)
Amikacin	
No	104 (68.87%)
Yes	47 (31.13%)
Cefotaxime	
No	145 (96.03%)
Yes	6 (3.97%)
Meropenem	
No	150 (99.34%)
Yes	1 (0.66%)

Characteristics	n (%)
Vancomycin	
No	151 (0.00%)
Yes	0 (0.00%)
Other antibiotics	
No	149 (98.68%)
Yes	2 (1.32%)
Pathogen Isolated	
Group B *Streptococcus*	
No	109 (72.19%)
Yes	0 (0.00%)
Not Done	42 (27.81%)
Escherichia coli	
No	109 (72.19%)
Yes	0 (0.00%)
Not Done	42 (27.81%)
Staphylococcus	
No	107 (70.86%)
Yes	2 (1.32%)
Not Done	42 (27.81%)
Listeria monocytogenes	
No	109 (72.19%)
Yes	0 (0.00%)
Not Done	42 (27.81%)
Pseudomonas	
No	109 (72.19%)
Yes	0 (0.00%)
Not Done	42 (27.81%)
Burkholderia	
No	109 (72.19%)
Yes	0 (0.00%)
Not Done	42 (27.81%)
Klebsiella	
No	109 (72.19%)
Yes	0 (0.00%)
Not Done	42 (27.81%)
Other bacteria	
No	107 (70.86%)
Yes	2 (1.32%)
Not Done	42 (27.81%)

Characteristics	n (%)
Complete Blood Count	
Anemia	
No	109 (72.19%)
Yes	14 (9.27%)
Not Done	28 (18.54%)
Leukopenia	
No	120 (79.47%)
Yes	3 (1.99%)
Not Done	28 (18.54%)
Leukocytosis	
No	117 (77.48%)
Yes	6 (3.97%)
Not Done	28 (18.54%)
High Absolute Neutrophil Count	
No	61 (40.40%)
Yes	62 (41.06%)
Not Done	28 (18.54%)
Low Absolute Neutrophil Count	
No	121 (80.13%)
Yes	2 (1.32%)
Not Done	28 (18.54%)
Thrombocytopenia	
No	118 (78.15%)
Yes	5 (3.31%)
Not Done	28 (18.54%)
Symptoms	
Poor suck	
No	145 (96.03%)
Yes	6 (3.97%)
Decreased activity	
No	146 (96.69%)
Yes	5 (3.31%)
Respiratory distress	
No	117 (77.48%)
Yes	34 (22.52%)
Hypo or hyperthermia	
No	150 (99.34%)
Yes	1 (0.66%)
Hypo or hyperglycemia	

Characteristics	n (%)
No	150 (99.34%)
Yes	1 (0.66%)
Hyperbilirubinemia	
No	115 (76.16%)
Yes	36 (23.84%)
Other symptoms	
No	134 (88.74%)
Yes	17 (11.26%)
Culture positive	
No	147 (97.35%)
Yes	4 (2.65%)

Table 3. Clinical outcomes of the neonates born to mothers with UTI (n=151).

Outcomes	n (%)
Age of Gestation	
Not preterm >37 weeks	118 (78.15%)
Preterm <37 weeks	33 (21.85%)
Clinical Sepsis	
No	89 (58.94%)
Yes	62 (41.06%)

of having preterm neonates compared to those who did not have kidney disease. Ampicillin (aPR 3.26, 95% CI: 1.31–8.07) was associated with a threefold increase in the risk of preterm neonates. This may be due to the ineffectiveness of ampicillin in treating the mother's infection, likely because of the prevalence of ampicillin-resistant bacteria, thereby potentially increasing the risk of transmitting the infection to the neonate. For the other bacteria, data indicated a significant association with clinical outcomes, showing an extremely high aPR for preterm births. Specifically, other bacteria were associated with an aPR of 322087.1 (95% CI: 10305.6 – 1.01e+07) for the risk of having a preterm neonate, suggesting a potential outlier or rare event with substantial impact. For the risk of clinical sepsis, significant predictors included maternal age, autoimmune disease, and kidney disease. Mothers aged 20-35 years had a significantly lower risk (aPR 0.46, 95% CI: 0.22–0.97) compared to those aged less than 19 years. Specifically, mothers aged 20-35 years were 56% more likely not to give birth to neonates with clinical sepsis compared to those mothers aged less than 19 years old. Maternal autoimmune disease with an aPR of 3.05 (95% CI: 1.81–5.11) and maternal kidney disease with an aPR of 3.60 (95% CI: 2.02–6.41) were also significant predictors, translating to a three-fold increased risk of giving birth to neonates with clinical sepsis, compared to those mothers without such comorbidities. Lastly, for other bacteria, for the risk of having clinical sepsis, the APR was 3.59e-08 (95% CI: 3.11e-09 – 4.15e-07), indicating an extremely low risk, likely reflecting the complexity and rarity of these bacterial infections in the study cohort. The appendix also presents the STATA output.

DISCUSSION

The study's findings offer crucial insights into the demographic and clinical characteristics of mothers with UTIs and their implications for maternal and neonatal health. The high prevalence of UTIs among mothers aged 20-35 years aligns with existing literature (Al-Badaii, et al, 2023; Nwachukwu, et

Table 4. Association between maternal characteristics and clinical outcomes of the neonates born to mothers with UTI for the risk of having preterm and clinical sepsis, measured at a 95% confidence interval (95% CI).

Maternal Characteristics	Clinical Neonatal Outcomes (adjusted Prevalence Ratio with a 95% CI)	
	Risk of Having Preterm Neonate	Risk of Having Clinical Sepsis
Maternal Age, years		
≤19 years old	1.00	1.00
20-35 years old	0.20 (0.05 – 0.84)	0.46 (0.22 – 0.97)
≥ 36 years old	0.22 (0.04 – 1.17)	0.53 (0.21 – 1.28)
Comorbidities		
Diabetes		
No	1.00	1.00
Yes	0.61 (0.24 – 1.50)	0.96 (0.61 – 1.52)
Hypertension		
No	1.00	1.00
Yes	1.61 (0.67 – 3.87)	1.37 (0.86 – 2.21)
Premature rupture of membranes (PROM)		
No	1.00	1.00
Yes	1.35 (0.46 – 3.98)	0.99 (0.51 – 1.93)
Autoimmune Disease		
No	1.00	1.00
Yes	<0.001 (<0.001 - <0.001)	3.05 (1.81 – 5.11)
Kidney Disease		
No	1.00	1.00
Yes	14.30 (3.91 – 52.24)	3.60 (2.02 – 6.41)
Presence of other comorbidities		
No	1.00	1.00
Yes	1.60 (0.67 – 3.80)	0.87 (0.50 – 1.52)
Obstetrics History		
Gravidity		
1	1.00	1.00
2-4	0.61 (0.16 – 2.35)	0.80 (0.33 – 1.91)
>5	<0.001 (<0.001 - <0.001)	0.45 (0.06 – 3.18)
Parity		
1	1.00	1.00
2-4	2.54 (0.66 – 9.81)	1.06 (0.43 – 2.63)
>5	<0.001 (<0.001 - <0.001)	6.13 (0.77 – 49.15)
Mode of Delivery		
Vaginal	1.00	1.00
Caesarian	0.50 (0.26 – 0.97)	0.73 (0.47 – 1.13)
Antibiotic Intake		
Amoxicillin		
No	1.00	1.00
Yes	3.64 (0.35 – 37.77)	1.85 (0.39 – 8.70)
Co-Amoxiclav		
No	1.00	1.00
Yes	0.70 (0.08 – 6.37)	0.63 (0.15 – 2.67)
Ampicillin		
No	1.00	1.00
Yes	3.26 (1.31 – 8.07)	1.44 (0.84 – 2.49)
Cephalexin		
No	1.00	1.00
Yes	<0.001 (<0.001 - <0.001)	<0.001 (<0.001 - <0.001)

Maternal Characteristics	Clinical Neonatal Outcomes (adjusted Prevalence Ratio with a 95% CI)	
	Risk of Having Preterm Neonate	Risk of Having Clinical Sepsis
Cefuroxime		
No	1.00	1.00
Yes	1.28 (0.12 – 13.14)	0.74 (0.16 – 3.63)
Cefixime		
No	1.00	1.00
Yes	<0.001 (<0.001 - <0.001)	<0.001 (<0.001 - <0.001)
Metronidazole		
No	1.00	1.00
Yes	1.38 (0.47 – 4.08)	1.06 (0.56 – 1.99)
Cefazolin		
No	1.00	1.00
Yes	<0.001 (<0.001 - <0.001)	0.83 (0.15 – 4.50)
Other antibiotics		
No	1.00	1.00
Yes	0.69 (0.15 – 3.27)	1.03 (0.39 – 2.70)
Most Dominant Pathogen		
Escherichia coli		
No	1.00	1.00
Yes	<0.001 (<0.001 - <0.001)	2.36 (0.62 – 8.99)
Not done	0.90 (0.17 – 4.79)	0.83 (0.40 – 1.72)
Other bacteria		
No	1.00	1.00
Yes	322087.1 (10305.6 – 1.01e+07)	3.59e-08 (3.11e-09 – 4.15e-07)
Not done	-	

al, 2018), which indicates that UTIs are common in women of reproductive age due to physiological changes during pregnancy that predispose them to infections. The significant incidence of comorbidities such as diabetes and hypertension is noteworthy because these conditions are known to complicate pregnancies and increase the risk of adverse outcomes (Gordin, et al, 2014; Sullivan, et al, 2011), including preterm birth and maternal morbidity. The high number of cesarean deliveries compared to vaginal births in this group is significant. This trend may be due to the health problems related to urinary tract infections during pregnancy, which might require surgery to avoid more complications for the mother and baby. While cesarean delivery is often necessary for medical reasons, it comes with risks such as higher chances of infection and longer recovery times compared to vaginal delivery (Gundersen, et al, 2018; Leth, et al, 2009). The significant use of Cefuroxime as an antibiotic treatment reflects current clinical guidelines favoring its use due to its efficacy and safety profile during pregnancy (Stojanova, et al, 2022). However, the low detection rates of pathogens such as Escherichia coli, despite being a common cause of UTIs, suggest potential issues with diagnostic practices or reporting. This highlights the need for improved microbiological testing to guide appropriate antibiotic therapy.

The study's results also emphasize the demographic and clinical traits of newborns born to mothers with UTI and their clinical outcomes. The data revealed a higher proportion of male neonates compared to female neonates. This finding aligns with existing literature which frequently notes a slightly higher male presence in newborn populations, possibly due to sex-linked biological differences in susceptibility to infections and other perinatal complications (Del Principe, et al, 2013; Lorente-Pozo, et al, 2018). Please take note of the following text: Apgar scores, which are a critical indicator of neonatal health immediately post-birth, were predominantly high in this study. 95.36% scored between 7 and 10 at the first minute, 98.01% at the fifth minute, and 100% at the tenth minute. These results suggest that most neonates were in good health at birth despite maternal UTI. This is consistent with other studies, indicating that

with appropriate management, maternal infections do not necessarily result in poor neonatal Apgar scores (Anggondowati, et al, 2017; Jansen, et al, 2020). Regarding birthweight, most neonates were classified as normal birthweight, while 25.17% were LBW. The incidence of LBW in this cohort is slightly higher than the average for the general population (Siza, 2008). Antibiotics commonly used in neonates include gentamicin and ampicillin, reflecting standard treatment for suspected neonatal infections. The prevalent use of amikacin also indicates its importance in treating neonates in this context (Muller-Pebody, et al, 2011). The identified pathogens, primarily Group B Streptococcus and Escherichia coli, are consistent with common causative agents of neonatal infections reported in the literature (Tiskumara, et al, 2009). However, the absence of pathogen testing in 27.81% of cases suggests a requirement for more thorough diagnostic efforts. The documented symptoms of sepsis illustrate the wide range of clinical presentations of neonatal sepsis. The rate of culture-positive sepsis was relatively low at 2.65%, which could indicate effective early intervention and antibiotic therapy in the mothers, a conclusion supported by similar studies (Karmila, et al, 2022; Theil, et al, 2020).

The clinical outcomes indicated that the majority of newborns were born at term, with a gestational age of over 37 weeks. This is reassuring and suggests that with proper management, maternal UTIs do not necessarily lead to preterm births, which is a conclusion supported by previous research (Abou Heidar, et al, 2019). The occurrence of clinical sepsis in 41.06% of neonates is concerning and emphasizes the importance of closely monitoring and managing these infants. Furthermore, factors not covered in this research, such as prematurity, ABO incompatibility leading to hyperbilirubinemia, congenital heart disease, and maternal infections like the flu, may also impact the patient's clinical course. These factors highlight the complexity of neonatal outcomes and the need for comprehensive care and thorough evaluation of all potential risk factors.

The association between maternal characteristics and neonatal clinical outcomes in mothers with UTIs is a critical area of investigation, given the potential implications for maternal and neonatal health. For preterm births, maternal age is a significant factor, with mothers aged 20-35 years having a much lower risk compared to those aged under 19 years. This is supported by existing literature indicating that teenage pregnancies are linked to higher risks of adverse neonatal outcomes, including preterm births (Karataşlı, et al, 2019; Smith & Pell, 2001). Additionally, kidney disease is identified as a strong predictor, consistent with previous research highlighting its detrimental effects on pregnancy outcomes (Cabiddu, et al, 2016; Hladunewich, 2017). Taking ampicillin, an antibiotic, is linked to a higher risk of preterm births. This is likely because ampicillin may not effectively treat serious infections caused by ampicillin-resistant bacteria. Infections during pregnancy can cause inflammation, weaken the amniotic membranes, or trigger uterine contractions, all of which can lead to preterm labor (Burdet, et al, 2014). Additionally, severe infections may affect placental function, reducing oxygen and nutrient supply to the fetus, further complicating the pregnancy, and increasing the likelihood of early delivery (Weckman, et al, 2019). While antibiotics are crucial in treating these infections, they can disrupt the natural bacterial balance, potentially causing conditions like bacterial vaginosis, which is also linked to preterm labor (Basavaprabhu, et al, 2020). Hence, the link between taking antibiotics and preterm births mainly stems from the severity of the infections being treated, rather than the antibiotics themselves directly causing preterm births. This is particularly true for the use of ampicillin. The ineffectiveness of ampicillin in treating the mother's infection, possibly due to the prevalence of ampicillin-resistant bacteria, may increase the risk of transmitting the infection to the baby.

Regarding clinical sepsis in neonates, maternal age again plays a significant role. Mothers aged 20-35 years have a lower risk compared to younger mothers, reinforcing the vulnerability of younger maternal age groups to adverse neonatal outcomes (Kang, et al, 2015). Maternal autoimmune disease and kidney disease are also significant predictors, indicating higher risks of neonatal infections and complications. This supports the established understanding that maternal comorbidities, particularly chronic diseases, are associated with higher risks (Brown, et al, 2022). The data showed a significant association between the presence of certain bacteria and clinical outcomes. Specifically, there is a high aPR for preterm births and a low aPR for clinical sepsis. These findings emphasize the importance of closely monitoring and managing less common bacterial pathogens during pregnancy. Even though these pathogens are rare, their presence can still result in significant adverse outcomes.

The findings of this study highlight the importance of maternal health and age in determining the outcomes for newborns in pregnancies complicated by UTIs. Maternal kidney disease and autoimmune conditions have a significant impact on neonatal health outcomes, emphasizing the need for careful prenatal care and tailored management strategies for these high-risk groups to reduce adverse outcomes. These results add to the growing evidence that emphasizes the crucial relationship between maternal characteristics and neonatal health, calling for increased clinical awareness and intervention strategies when managing pregnancies complicated by UTIs (Abou Heidar, et al, 2019).

The practical clinical applications of understanding the association between maternal characteristics and neonatal clinical outcomes in mothers with UTIs are profound. Recognizing maternal age as a significant factor, particularly the increased risk in mothers under 19 years, underscores the need for targeted interventions for teenage pregnancies to prevent preterm births. Healthcare providers should be vigilant in managing teenage pregnancies and implementing rigorous monitoring and support systems. Furthermore, the identification of maternal kidney disease as a strong predictor of adverse neonatal outcomes necessitates specialized prenatal care protocols for affected mothers, including closer monitoring and early interventions to mitigate risks. The relationship between antibiotic use, specifically ampicillin, and preterm births highlights the necessity for careful antibiotic stewardship and the consideration of potential adverse effects on pregnancy outcomes. Clinicians must balance the need for treating severe infections with the potential impact on preterm labor, ensuring appropriate antibiotic use and monitoring for complications like bacterial vaginosis. Additionally, the increased risk of neonatal sepsis associated with younger maternal age and maternal comorbidities, such as autoimmune and kidney diseases, calls for tailored care plans for these high-risk groups. This includes comprehensive prenatal screening and management strategies to reduce the incidence of neonatal infections. Overall, these findings advocate for enhanced clinical awareness and the development of intervention strategies to improve maternal and neonatal health outcomes in pregnancies complicated by UTIs, emphasizing the critical role of personalized and vigilant prenatal care.

This study has strengths such as the thorough analysis of various maternal characteristics and their connections to neonatal outcomes. It offers detailed insights into how factors like maternal age, comorbidities, and antibiotic use impact preterm births and clinical sepsis. The study's focus on mothers with UTIs provides valuable insights for managing high-risk pregnancies, which can lead to improved prenatal care practices and targeted interventions.

Despite these strengths, it is important to use the study results cautiously and acknowledge its limitations. One limitation is that the study relied on medical records for data collection, which may have resulted in incomplete or inaccurate information due to inconsistent documentation practices. Additionally, the sample size of 151 individuals may not be large enough to generalize the findings broadly. This is further complicated by the overrepresentation of mothers aged 20-35 years and the limited representation of younger and older age groups, which could skew the results and limit their applicability to a more diverse population. The retrospective nature of the study prevents establishing causality between maternal UTIs and neonatal outcomes, as only associations can be inferred. Additionally, the low detection rates of pathogens such as Escherichia coli indicate potential issues with diagnostic accuracy or reporting practices. Furthermore, the high percentage of cases with no pathogen testing further emphasizes the need for more comprehensive and systematic microbiological testing. In light of these methodological constraints, it is essential to interpret the results cautiously. Further research with larger, more diverse samples and prospective designs is necessary to validate these findings and enhance their clinical relevance.

CONCLUSION AND RECOMMENDATIONS

This study investigates the link between maternal characteristics and neonatal clinical outcomes in mothers with UTIs. The findings highlight important factors such as maternal age, kidney disease, and antibiotic use, which play a crucial role in understanding the risks of preterm births and clinical sepsis in babies. Younger maternal age and the presence of comorbidities like kidney disease significantly raise the risk of adverse neonatal outcomes, underscoring the need for targeted interventions and careful prenatal care. The study also emphasizes the importance of improved diagnostic practices, especially in pathogen detection, in managing and treating UTIs during pregnancy.

Based on these findings, several recommendations are proposed. Firstly, healthcare providers should implement targeted intervention programs for teenage pregnancies to reduce the higher risks of preterm births and clinical sepsis. Additionally, specialized prenatal care protocols should be developed for mothers with kidney disease and other significant comorbidities to ensure closer monitoring and early intervention, thus improving maternal and neonatal outcomes. Emphasizing antibiotic stewardship programs is crucial to balance effective infection management with potential risks associated with antibiotic use during pregnancy. Finally, enhancing microbiological testing and diagnostic accuracy is essential to guide appropriate treatment decisions and improve care for pregnant women with UTIs.

It is recommended to conduct long-term studies with larger and more diverse populations for future research in order to validate these findings and further explore causal relationships. Investigating the lasting effects of UTIs and associated treatments on both mothers and their infants would provide valuable insights into the extended impact of these infections. Additionally, researching the development and efficacy of targeted intervention programs for high-risk groups, such as teenage mothers and those with chronic conditions, would be beneficial. Exploring innovative diagnostic methods and antibiotic alternatives could also improve the management and outcomes of UTIs during pregnancy. These future research directions aim to build on the current study's findings and contribute to the broader understanding and improvement of maternal and neonatal health.

REFERENCES

Abou Heidar NF, Degheili JA, Yacoubian AA & Khauli RB. Management of urinary tract infection in women: A practical approach for everyday practice. Urology Annals 2019; 11(4): 339-46.

Ahmad H & Halim H. Determining sample size for research activities. Selangor Bus Rev 2017; 20-34.

Al-Adnani M & Sebire N. The role of perinatal pathological examination in subclinical infection in obstetrics. Best Practice & Research Clin Obstet Gynaecol 2007; 21(3): 505-21.

Al-Badaii F, Al-Tairi M, Rashid A, Al-Morisi S & Al-Hamari N. Prevalence, risk factors and antibiotic susceptibility of urinary tract infections among pregnant women: A study in Damt District Yemen. J Pure Applied Microbiol 2023; 17(2).

Al-Mamoryi NA & Al-Salman AS. Prevalence of symptomatic urinary tract infections and asymptomatic bacteriuria in Iraqi pregnant women of Babylon Governorate. Med J Babylon 2019; 16(1): 5-12.

Alam MM, Saleem AF, Shaikh AS, Munir O & Qadir M. Neonatal sepsis following prolonged rupture of membranes in a tertiary care hospital in Karachi, Pakistan. J Infect Dev Countr 2014; 8(01): 067-73.

Alemu A, Moges F, Shiferaw Y, Tafess K, KassuA, Anagaw B & Agegn A. Bacterial profile and drug susceptibility pattern of urinary tract infection in pregnant women at University of Gondar Teaching Hospital, Northwest Ethiopia. BMC Res Notes 2012; 5: 1-7.

Alexander JM, McIntire DM & Leveno KJ. Chorioamnionitis and the prognosis for term infants. Obstet Gynecol 1999; 94(2): 274-8.

Allen SR. Urinary tract infections in pregnancy. Clin Matern Fet Med 2021; 71-7 CRC Press.

Anggondowati T, El-Mohandes AA, Qomariyah SN, et al. Maternal characteristics and obstetrical complications impact neonatal outcomes in Indonesia: a prospective study. BMC Pregn Childbirth 2017; 17: 1-12.

Basavaprabhu H, Sonu K & Prabha R. Mechanistic insights into the action of probiotics against bacterial vaginosis and its mediated preterm birth: An overview. Microb Pathog 2020; 141: 104029.

Belete MA & Saravanan M. A systematic review on drug resistant urinary tract infection among pregnant women in developing countries in Africa and Asia; 2005–2016. Infect Drug Res 2020; 1465-77.

Bolton M, Horvath Jr DJ, Li B, Cortado H, Newsom D, White P, Partida-Sanchez S & Justice SS. Intrauterine growth restriction is a direct consequence of localized maternal uropathogenic Escherichia coli cystitis. PloS One 2012; 7(3): e33897.

Brown HK, McKnight A, & Aker A. Association between pre-pregnancy multimorbidity and adverse maternal outcomes: a systematic review. J Multimorb Comorb 2022; 12: 26335565221096584.

Buka SL, Tsuang MT, Torrey EF, Klebanoff MA, Bernstein D & Yolken RH. Maternal infections and subsequent psychosis among offspring. Arch Gen Psychiatr 2001; 58(11): 1032-7.

Burdet J, Dominguez P, Rubio A, Ines Salazar A, Laura Ribeiro M, Ibarra C & Maria Franchi A. Inflammation, infection and preterm birth. Curr Pharmaceut Design 2014; 20(29): 4741-8.

Cabiddu G, Castellino S, Gernone G, et al. A best practice position statement on pregnancy in chronic kidney disease: the Italian Study Group on Kidney and Pregnancy. J Nephrol 2016; 29: 277-303.

Cochran, WG & Chambers SP. The planning of observational studies of human populations. J Royal Stat Soc. Series A (General) 1965; 128(2): 234-66.

Del Principe D, Marconi M, Matarrese P, Villani A & Malorni W. Gender disparity in pediatric diseases. Curr Mol Med 2013; 13(4): 499-513.

Dauby N, Goetghebuer T, Kollmann TR, Levy J & Marchant A. Uninfected but not unaffected: chronic maternal infections during pregnancy, fetal immunity, and susceptibility to postnatal infections. Lancet Infect Dis 2012; 12(4): 330-40.

Delzell Jr, JE & Lefevre ML. Urinary tract infections during pregnancy. Am Fam Phys 2000; 61(3): 713-20.

Ejerssa AW, Gadisa DA & Orjino TA. Prevalence of bacterial uropathogens and their antimicrobial susceptibility patterns among pregnant women in Eastern Ethiopia: hospital-based cross-sectional study. BMC Women's Health 2021; 21(1): 291.

El-Kashif MML. Urinary tract infection among pregnant women and its associated risk factors: A cross-sectional study. Biomed Pharmacol J 2019; 12(4): 2003-2010.

Emamghorashi F, Mahmoodi N, Tagarod Z & Heydari ST. Maternal urinary tract infection as a risk factor for neonatal urinary tract infection 2012.

Emiru T, Beyene G, Tsegaye W & Melaku S. Associated risk factors of urinary tract infection among pregnant women at Felege Hiwot Referral Hospital, Bahir Dar, North West Ethiopia. BMC Res Notes 2013; 6: 1-6.

Etafa W, Fetensa G, Tsegaye R, Wakuma B, Sundararajan V, Bayisa G & Turi E. Neonatal sepsis risk factors in public hospitals in Wollega zones, Ethiopia: case control study. PAMJ-One Health 2022; 7(2).

Geerlings SE. Clinical presentations and epidemiology of urinary tract infections. Microbiol Spect 2016; 4(5): 4.5. 03.

Gilbert NM, O'brien VP, Hultgren S, Macones G, Lewis WG & Lewis AL. Urinary tract infection as a preventable cause of pregnancy complications: opportunities, challenges, and a global call to action. Global Adv Health Med 2013; 2(5): 59-69.

Gillenwater JY. Pathophysiology of obstructive uropathy. Prevention of Kidney and Urinary Tract Disease 1978; DHEW (NIH 78-855), 5, 169-187.

Goldenberg RL, Hauth JC & Andrews WW. Intrauterine infection and preterm delivery. New Engl J Med 2000; 342(20): 1500-7.

Gordin D, Forsblom C, Groop PH, Teramo K & Kaaja R. Risk factors of hypertensive pregnancies in women with diabetes and the influence on their future life. Ann Med 2014; 46(7): 498-502.

Gundersen TD, Krebs L, Loekkegaard ECL, Rasmussen SC, Glavind J & Clausen TD. Postpartum urinary tract infection by mode of delivery: a Danish nationwide cohort study. BMJ Open 2018; 8(3): e018479.

Haque K, Chagia AH & Shaheed M. Half a decade of neonatal sepsis, Riyadh, Saudi Arabia. J Trop Pediatr 1990; 36(1): 20-3.

Haque KN. Defining common infections in children and neonates. J Hospital Infect 2007; 65: 110-4.

Hladunewich MA. Chronic kidney disease and pregnancy. Seminars in Nephrology 2017.

Hutton EK & Thorpe J. Consequences of meconium stained amniotic fluid: what does the evidence tell us? Early Human Development 2014; 90(7): 333-9.

Jansen S, Lopriore E, Naaktgeboren C, Sueters M, Limpens J, Van Leeuwen E & Bekker V. Epidural-related fever and maternal and neonatal morbidity: a systematic review and meta-analysis. Neonatology 2020; 117(3): 259-70.

John AS, Mboto CI & Agbo B. A review on the prevalence and predisposing factors responsible for urinary tract infection among adults. Euro J Exp Bio 2016; 6(4): 7-11.

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(4): 448-53.

Kang G, Lim JY & Kale AS. Adverse effects of young maternal age on neonatal outcomes. Singapore Med J 2015; 56(3): 157.

Karataslı V, Kanmaz AG, İnan AH, Budak A & Beyan E. Maternal and neonatal outcomes of adolescent pregnancy. J Gynecol Obstet Hum Reprod 2019; 48(5): 347-50.

Karmila A, Barchia I, Ramandati A & Zhang L. Clinical and bacteriological profile of culture-negative and culture-proven neonatal sepsis in Palembang, Indonesia. J Infect Dev Countr 2022; 16(12): 1887-96.

Kaufman D & Fairchild KD. Clinical microbiology of bacterial and fungal sepsis in very-low-birth-weight infants. Clin Microbiol Rev 2004; 17(3): 638-80.

Korb A, Barimacker S, dos Santos M, Fincatto S, Vendruscolo C, Menegatti M & Cabral D. Risk factors to urinary tract infection related to prenatal care in pregnancy women attending public care units of South Brazil. J Preg Child Health 2018; 5(6).

Kumar M, Saadaoui M & Al Khodor S. Infections and pregnancy: Effects on maternal and child health. Frontiers in Cellular and Infection Microbiology 2022; 690.

Laari JL, Anab M, Jabong DP, Abdulai K & Alhassan AR. Maternal age and stage of pregnancy as determinants of UTI in pregnancy: A case of Tamale, Ghana. Infect Dis Obstet Gynecol 2022.

Leth RA, Møller JK, Thomsen RW, Uldbjerg N & Nørgaard M. Risk of selected postpartum infections after cesarean section compared with vaginal birth: a five-year cohort study of 32,468 women. Acta Obstetricia et Gynecologica Scandinavica 2009; 88(9): 976-83.

Lindholm J. Plasma and urinary cortisol in pregnancy and during estrogen-gestagen treatment. Scandinavian J Clin Lab Invest 1973; 31(1): 119-22.

Loh KY & Sivalingam N. Urinary tract infections in pregnancy. Malaysian Fam Phys 2007; 2(2): 54.

Lorente-Pozo S, Parra-Llorca A, Torres B, Torres-Cuevas I, Nuñez-Ramiro A, Cernada M, García-Robles A & Vento M. Influence of sex on gestational complications, fetal-to-neonatal transition, and postnatal adaptation. Frontiers in Pediatr 2018; 6: 63.

Mathur MB, Ding P, Riddell CA & VanderWeele TJ. Website and R package for computing E-values. Epidemiology (Cambridge, Mass.) 2018; 29(5): e45.

Matuszkiewicz-Rowińska J, Małyszko J & Wieliczko M. State of the art paper Urinary tract infections in pregnancy: old and new unresolved diagnostic and therapeutic problems. Arch Med Sci 2015; 11(1): 67-77.

McGrady GA, Daling JR & Peterson DR. Maternal urinary tract infection and adverse fetal outcomes. Am J Epidemiol 1985; 121(3): 377-81.

Muglia LJ, & Katz M. The enigma of spontaneous preterm birth. New England J Med 2010; 362(6): 529-35.

Muller-Pebody B, Johnson A, Heath P, Gilbert R, Henderson K, Sharland M & Group i. Empirical treatment of neonatal sepsis: are the current guidelines adequate? Arch Dis Childhood-Fetal and Neonatal Edition 2011; 96(1): F4-F8.

Newman M, Frimpong E, Asamoah-Adu A & Sampene-Donkor E. Resistance to antimicrobial drugs in Ghana. The Ghanaian-Dutch Collaboration for Health Research and Development. Project number 2001. 2006.

Nteziyaremye J, Iramiot SJ, Nekaka R, Musaba MW, Wandabwa J, Kisegerwa E & Kiondo P. Asymptomatic bacteriuria among pregnant women attending antenatal care at Mbale Hospital, Eastern Uganda. PloS One 2020; 15(3): e0230523.

Nwachukwu E, Onyebuchi O & Michael O. Prevalence of urinary tract infections in pregnant women in Onitsha, Nigeria. J Bacteriol Mycol Open Access 2018; 6(5): 284-5.

Ornoy A & Tenenbaum A. Pregnancy outcome following infections by coxsackie, echo, measles, mumps, hepatitis, polio and encephalitis viruses. Reprod Toxicol 2006; 21(4): 446-57.

Piantino JH, Schreiber MD, Alexander K & Hageman J. Culture negative sepsis and systemic inflammatory response syndrome in neonates. NeoReviews 2013; 14(6): e294-e305.

Pradhan J, Mallick S, Mishra N, Tiwari A & Negi VD. Pregnancy, infection, and epigenetic regulation: A complex scenario. Biochimica et Biophysica Acta (BBA)-Molecular Basis of Disease 2023; 166768.

Rafi MA, Miah MMZ, Wadood MA & Hossain MG. Risk factors and etiology of neonatal sepsis after hospital delivery: a case-control study in a tertiary care hospital of Rajshahi, Bangladesh. PloS One 2020; 15(11): e0242275.

Redman CW, Sacks GP & Sargent IL. Preeclampsia: an excessive maternal inflammatory response to pregnancy. Am J Obstet Gynecol 1999; (2): 499-506.

Riley C & Wheeler DS. Prevention of sepsis in children: a new paradigm for public policy. Crit Care Res Pract 2012.

Sampaio AFS, Rocha MJFd & Leal EAS. High-risk pregnancy: clinical-epidemiological profile of pregnant women attended at the prenatal service of the Public Maternity Hospital of Rio Branco, Acre. Revista Brasileira de Saúde Materno Infantil 2018; 18: 559-66.

Schnarr J & Smaill F. Asymptomatic bacteriuria and symptomatic urinary tract infections in pregnancy. Eur J Clin Invest 2008; 38: 50-7.

Seyoum K, Sahiledengle B, Kene C, Geta G, Gomora D, Ejigu N, Mesfin T & Chattu VK. Determinants of neonatal sepsis among neonates admitted to neonatal intensive care units in ethiopian hospitals: A systematic review and meta-analysis. Heliyon 2023.

Sharma P & Thapa L. Acute pyelonephritis in pregnancy: a retrospective study. Austr New Zealand J Obstet Gynaecol 2007; 47(4): 313-5.

Sibi G, Kumari P & Kabungulundabungi N. Antibiotic sensitivity pattern from pregnant women with urinary tract infection in Bangalore, India. Asian Pacific J Trop Med 2014; 7: S116-S120.

Siza J. Risk factors associated with low birth weight of neonates among pregnant women attending a referral hospital in northern Tanzania. Tanzania J Health Res 2008; 10(1): 1-8.

Smith GC & Pell JP. Teenage pregnancy and risk of adverse perinatal outcomes associated with first and second births: population based retrospective cohort study. BMJ 2001; 323(7311): 476.

Spiegelman D & Hertzmark E. Easy SAS calculations for risk or prevalence ratios and differences. Am J Epidemiol 2005; 162(3): 199-200.

Stojanova J, Arancibia M, Ghimire S & Sandaradura I. Understanding the pharmacokinetics of antibiotics in pregnancy: Is there a role for therapeutic drug monitoring? A narrative review. Ther Drug Monit 2022; 44(1): 50-64.

SullivanSD, Umans JG & Ratner R. Hypertension complicating diabetic pregnancies: pathophysiology, management, and controversies. J Clin Hypertens 2011; 13(4), 275-84.

Tamhane AR, Westfall AO, Burkholder GA & Cutter GR. Prevalence odds ratio versus prevalence ratio: choice comes with consequences. Stat Med 2016; 35(30): 5730-5.

Teeguarden JG, Twaddle NC, Churchwell MI & Doerge DR. Urine and serum biomonitoring of exposure to environmental estrogens I: Bisphenol A in pregnant women. Food Chem Toxicol 2016; 92: 129-42.

Terblanche M, Almog Y, Rosenson RS, Smith TS, & Hackam DG. Statins and sepsis: multiple modifications at multiple levels. Lancet Infect Dis 2007; 7(5): 358-68.

Theil C, Freudenberg SC, Gosheger G, Schmidt-Braekling T, Schwarze J & Moellenbeck B. Do positive cultures at second stage re-implantation increase the risk for reinfection in two-stage exchange for periprosthetic joint infection? J Arthroplasty 2020; 35(10): 2996-3001.

Tiskumara R, Fakharee S, Liu C, et al. Neonatal infections in Asia. Arch Dis Childhood-Fetal and Neonatal Edition 2009; 94(2): F144-8.

Towers CV, Yates A, Zite N, Smith C, Chernicky L & Howard B. Incidence of fever in labor and risk of neonatal sepsis. Am J Obstet Gynecol 2017; 216(6): 5 e591-96.

Ullah MA, Barman A, Siddique M & Haque A. Prevalence of asymptomatic bacteriuria and its consequences in pregnancy in a rural community of Bangladesh. Bangladesh Med Res Council Bull 2007; 33(2): 60-4.

Urbaniak G & Plous S. Research randomizer (version 4.0) [computer software]. In. 2013

VanderWeele TJ & Ding P. (eds.): Sensitivity Analysis in Observational Research: Introducing the E-value. Ann Int Med 2013; 167(4): 268-74.

Vasudevan R. Urinary tract infection: an overview of the infection and the associated risk factors. J Microbiol Exp 2014; 1(2): 00008.

Vogel JP, Lee AC & Souza JP. Maternal morbidity and preterm birth in 22 low-and middle-income countries: a secondary analysis of the WHO Global Survey dataset. BMC Preg Childbirth 2014; 14: 1-14.

Weckman AM, Ngai M, Wright J, McDonald CR & Kain KC. The impact of infection in pregnancy on placental vascular development and adverse birth outcomes. Front Microbiol 2019; 10: 1924.

Woldu MA, Guta M, Lenjisa J, Tegegne G, Tesafye G & Dinsa H. Assessment of the incidence of neonatal sepsis, its risk factors, antimicrobial use and clinical outcomes in Bishoftu General Hospital. Neonatal Intensive Care Unit, Debrezeit-Ethiopia. Pediat Therapeut 2014; 4(214): 2161.

Zou G. A modified poisson regression approach to prospective studies with binary data. Am J Epidemiol 2004; 159(7): 702-6.