

Susceptibility Antibiotics of Bacteria Causing Urinary Tract Infection in Pregnant Women Infected with COVID-19

Rashid Rahim Hateet

Department of Biology, College of Sciences, University of Misan, Misan, Iraq

Abstract

Urinary tract infections (UTIs) are a significant issue in women of all ages, but they are especially common during pregnancy. Co-infection of the Coronavirus Disease 2019 (COVID-19) with UTIs in pregnant females is a hot topic today, as it may be linked to various conditions. Furthermore, understanding the types of bacteria that cause UTIs and related antimicrobial resistance may aid the clinician in selecting the appropriate empirical treatment. This study aimed to isolate and characterize causative agents of UTIs and determine antimicrobial treatment sensitivity patterns among pregnant women diagnosed with the COVID-19 admitted to Teaching Hospital X in Iraq. Antimicrobial drug resistance testing was performed on 42 mid-stream urine samples that had been prepared for culture. *Escherichia coli* (18/42.85%), *Klebsiella pneumoniae* (9/21.45%), *Streptococcus galactica* (7/16.66%), and *Proteus mirabilis* (4/9.52%) were the bacteria isolated and diagnosed from pregnant women. The infections *Pseudomonas aeruginosa* and *Staphylococcus aureus* were the least common (2/4.7). In conclusion, the isolated uro-pathogens showed high resistance to Gentamicin, Cefuroxime, Ceftriaxone and sensitive to Ampicillin and Nitrofurantoin. The common cause of UTIs among pregnant women infected with the COVID-19 was discovered to be *Escherichia coli*. Before recommending therapy, culture and sensitivity testing of isolates from urine tests should be conducted on a regular basis.

Keywords: antimicrobial susceptibility pattern, COVID-19, pregnant women, urinary tract infections

Introduction

The Coronavirus Disease 2019 (COVID-19) is gradually spreading globally, and the World Health Organization (WHO) declared the COVID-19 pandemic on March 11, 2020.¹ The first outbreak was discovered in Wuhan City, Hubei Province, China and quickly spread across the world.² The COVID-19 has resulted in about 420,000 confirmed patients and 18,887 deaths worldwide since around March 25, 2020, with 81,852 reported cases and 3,287 deaths in China.³ The COVID-19 outbreak and pregnancy in terms of clinical features and consequences were observed.⁴ The COVID-19 is especially dangerous for pregnant women who are older, obese or have post-medical issues like hypertension (high blood pressure) or diabetes mellitus.

Pregnant women infected with the COVID-19 require extra care. There is currently insufficient evidence on the COVID-19 and pregnancy, with most cases occurring late pregnancy, posing a danger to both the mother and fetus. A COVID-19-infected mother's late pregnancy may result in negative urological consequences. When working with some of these patients, an interdisciplinary

team approach should be used because it allows for the effective acquisition of information, skills, and responsibility.⁵

Urinary tract infections (UTIs) are frequent in pregnant women. Pyelonephritis is by far the most detected medically diagnosed condition in pregnancy, and it can present itself in that way as UTIs, with poor treatment leading to complications. As a result, practitioners must be able to tell the difference between the normal and abnormal urinary tract and kidney results, assess anomalies, and cure diseases.⁶

Urinary contamination was documented in nearly 10% of primary care appointments among expectant mothers, and thus more about 15% of women had a single episode of UTI at some point in their lives. UTIs frequently occur as a result of an escalating infection.⁷ Due to ureteral dilation, increased bladder capacity, and reduced bladder tone, as well as reduced ureteral timbre, which contributes to higher urine stagnation and ureterovesical reflux, pregnant people, are more likely to have UTIs. Glycosuria, which affects 70% of pregnant women, stimulates bacterial development in the urine.

Correspondence*: Rashid Rahim Hateet, Department of Biology, College of Sciences, University of Misan, Misan, Iraq, Email: biorashed@uomisan.edu.iq, Phone: +96 477 1613 4011

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With significant functional physiological and hormonal variations, as well as the position of the inguinal mucous, pregnant women, are more susceptible to urinary tract infection. Bacterial infections found in rectal plants can now enter the vagina via the genitals.⁸ The *Enterococcus* family, which contains *E. coli*, *Klebsiella spp.*, *Proteus spp.*, and *Enterobacter spp.*, is the most common cause of bacterial infection. Inability to recognize bacteremia during pregnancy raises the risk of acute pyelonephritis by 25% and can lead to problems such as preterm birth, temporary kidney failure, pulmonary fibrosis, sepsis, shocks, and hematological disorders. Women who have an untreated UTI during their third trimester are already at risk of giving birth to a child with mental disorders or developmental delays.⁹ This study aimed to isolate and identify the bacteria causing UTIs in the COVID-19-infected pregnant women and then assess the impact of antibiotics on the microorganisms isolated from urine samples.

Method

A total of 42 samples of urine were collected from pregnant women infected with the COVID-19 at Teaching Hospital X in Misan City, Iraq. The age of patients was categorized into three groups: 25–30, 31–35, and 36–45 years old. A mid-stream urine sample was taken for each woman in sterilized test tubes for the period from February 2021 to July 2021. All samples were cultured on nutrient agar, MacConkey agar, 5% blood agar, mannitol salt agar and incubated overnight at 37°C aerobically for 24 hours.

All urine samples were examined under a microscope. First, colonies were diagnosed initially depending on the phenotypic and culture characteristics. Identification of the isolated bacteria was done according to standard microbiological methods,¹⁰ including cultural characters, and gram stain then isolates were diagnosed by VITEK® 2 Compact Automated Systems with ID-GN and ID-GP cards based on the manufactures instructions.

Antimicrobial susceptibility tests were performed using the Kirby–Bauer disk diffusion method recommended by the Clinical and Laboratory Standards Institute

(CLSI).¹¹ All aspects of the Kirby–Bauer procedure are standardized to ensure consistent and accurate results. The media used is Mueller-Hinton agar at only 4 mm deep, poured into either 100 mm or 150 mm Petri dishes. The pH level of the agar must be between 7.2 and 7.4. Bacterial inoculum is prepared by diluting a broth culture to match a 0.5 McFarland turbidity standard, which is equivalent to approximately 150 million cells per mL.¹² The antibiotics tested were Ampicillin, Amikacin, Ceftriaxone, Cefotaxime, Ciprofloxacin, Gentamicin, Erythromycin, Nalidixic, and Nitrofurantoin.

The statistical analysis of the obtained results was performed using the SAS statistical package v.9.2. Statistical analyses were based on the model of analysis of variance (ANOVA) and Tukey's multiple tests (or confidence interval) at the assumed significance level of 0.05. The statistical averages were compared according to the Least Significance Difference (LSD) test.²⁴

Results

A total of 42 urine samples were positively cultured. The result of this study showed the pathogen isolates and their respective percentage shown in Table 1; positive culture included the most frequent organism; *E. coli* (18/42.85%) followed by *Klebsiella pneumoniae* by nine isolates (21.45%), *Streptococcus galactica* (7/16.66%), and *Proteus mirabilis* (4/9.52%), *Pseudomonas aeruginosa* and *Staphylococcus aureus* were the least identified pathogens (2/4.7).

The age range for the selected samples was classified into three categories as shown in Table 2 in which the highest infected age is 36-45 years old represented by 30 isolates (71.42%) While, there was no difference between the age groups of 25-30 and 31-35 years. The UTI was determined based on the general urine lab examination including Pus Cells, RBCs, and Epithelial cells that revealed significant relationships between the bacterial isolates and the UTIs problems.

Figure 1 presents the number of pregnancies among the samples studied. The highest sector infected by identified bacteria was (4 to 5) by 20/47.61% followed by (1 to 3) by 15/37.71%, and finally, the least number of iso-

Table 1. Distribution of Bacteria Isolated from Urine Samples of Pregnant Women Presenting with Symptoms of Urinary Tract Infection and General Urine Examination

Bacterial Isolate	n	%	Pus Cell	RBC	Epithelial Cell
<i>Escherichia coli</i>	18	42.85	30	10	18
<i>Klebsiella pneumoniae</i>	9	21.45	22	2	20
<i>Streptococcus galactica</i>	7	16.66	18	2	18
<i>Proteus mirabilis</i>	4	9.52	16	4	14
<i>Pseudomonas aeruginosa</i>	2	4.76	15	2	14
<i>Staphylococcus aureus</i>	2	4.76	14	4	10
LSD at 0.05	1.779		1.751	1.699	1.677

Notes: RBCs = Red Blood Cells, LSD = Least Significant Difference

lated strains was for (6 to 7) by 7/165.6%. The result of this study also showed that the percentage of Gram-negative bacteria is higher than the percentage of Gram-positive bacteria (66.6%) (33.3%), respectively (Table 3).

Discussion

Urinary tract infections are among the most predominant infectious illnesses, impacting 150 million people across the globe each year.¹ In 2007, there had been approximately 10.5 million appointment visits for symptoms (representing 0.9% of all outpatient visits) and 2–3 million urgent care visits 2–4 in the United States alone. In the Western world solely, the societal costs of the diseases, including wellness costs and lost time at work, are conservatively believed to be around USD 3.5 billion each year. Urinary tract infections are quite a deadly disease in children, elderly men, and women of all ages.¹³

Urinary tract infection is a relatively prevalent condition and its early diagnosis has significant consequences for personal health, antimicrobial resistance, and medical expenses.¹⁴ Because the incidence of bacteria and their characteristics might fluctuate with temporal and spatial location, monitoring of local UTIs aetiology, as well as antibiotic susceptibility, is deemed valuable to guide temporal structure.¹⁵ Using demographic and clinical data, efforts should really be made to improve the prediction of causal uropathogens. Along with the worldwide COVID-19 pandemic, UTIs in pregnant women should be monitored and evaluated on a regular basis.

Urinary tract infections are caused by a variety of microorganisms, which includes both gram positive and gram-negative ones. In a study, *E. coli* (42.85%) was pre-

dominant isolate followed by *Klebsiella pneumoniae* (21.45%), *Streptococcus galactica* (16.66%), and *Proteus mirabilis* (9.52 %) respectively. This finding is similar to many reports indicating that gram-negative bacteria mostly *E. coli* and *Proteus spp.* are the most common pathogens isolated in a patient with UTIs. A study showed that 42 samples collected and screened from patients infected by the COVID-19 and UTIs yielded positive bacteria cultures and it has again confirmed UTIs to be a common infection in women.¹⁶ The UTI patients might have a correlation to the COVID-19 pandemic side effects or risk factors.

In this study, bacteria were gram-negative most common at 66.6% and the gram-positive bacteria at 33.3.1%. The incidents were found similar in rural areas of Tanzania.¹⁷ Gram-negative and gram-positive organisms, and certain other types of fungi, can cause UTIs. Uropathogenic *E. coli* diseases are the major cause of both simple and complex UTIs. *K. pneumoniae*, *S. saprophyticus*, *Streptococcus galactica*, *Proteus mirabilis*, *Pseudomonas aeruginosa*, *Staphylococcus aureus*, and *Candida spp.* are the most common agents involved in simple UTIs.^{3,6,12,13} This fact is clearly demonstrated in the current study in Table 3, *E. coli* was the main pathogenic isolated from urine samples accounting for 18 (42.8% out of all isolates) with big bacteremia. *E. coli* was to be a diuretic due to count of the factors of the spectra of colonialism invasion of urinary epithelium such as Adhesions fiber (P) and fiber (S).¹⁸ *Klebsiella pneumoniae* was the second most common isolated bacteria coagulant negative.

Urinary Tract Infection Relation to Age and the COVID-19 in Pregnant Women

Obviously, age is a risk factor that plays an important role in transmitting UTIs in pregnant women where 30 isolates out of 42 (71.42%) appeared in the age range of 36 to 45 years, whereas younger age was recorded with a low number of isolates (12 /-28.58%). This fact is in line with the study by Rowe and Mehta in 2013,¹⁹ who stated that in the elderly, UTIs and subclinical bacteriuria are prevalent It is difficult to tell the difference between a severe UTI and asymptomatic bacteriuria in older persons, especially those in long-term care institutions because

Table 2. Distribution of Isolates with Age Range and Their Respective Percentage

Age Range (years)	n	%
25-30	6	14.28
31-35	6	14.28
36-45	30	71.42

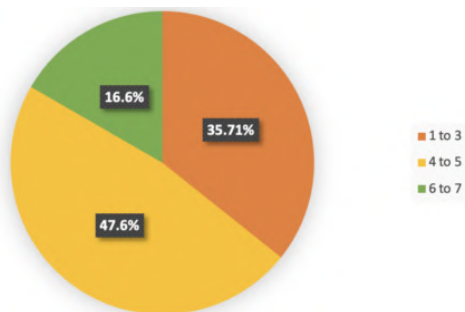


Figure 1. The Number of Pregnancies among the Samples Studied

Table 3. Gram-negative and Gram-positive Bacteria and Their Respective Percentage

Bacterial Isolate	Status	%
<i>Escherichia coli</i>	Negative	66.6%
<i>Klebsiella pneumoniae</i>	Negative	
<i>Proteus mirabilis</i>	Negative	
<i>Pseudomonas aeruginosa</i>	Negative	
<i>Staphylococcus aureus</i>	Positive	33.3%
<i>Streptococcus galactica</i>	Positive	

Table 4. Resistance of Organisms to Antibiotics (%)

Bacterial Isolate	Ampicillin	Amikacin	Ceftriaxone	Cefotaxime	Ciprofloxacin	Gentamicin	Erythromycin	Nalidixic	Nitrofurantoin	LSD at 0.05
<i>Escherichia coli</i>	27	24	55	80	78	80	22	26	38	2.33
<i>Klebsiella pneumoniae</i>	12	40	80	72	80	77	27	53	27	2.31
<i>Streptococcus galactica</i>	22	25	46	70	40	70	12	22	22	4.40
<i>Proteus mirabilis</i>	40	38	50	58	35	72	38	46	35	2.56
<i>Pseudomonas aeruginosa</i>	25	27	70	70	42	76	40	50	20	2.45
<i>Staphylococcus aureus</i>	40	30	22	82	50	82	20	70	35	3.21

they are less likely to have localized gynecologic symptoms.

Patients with urine incontinence and chronic intermittent cystitis/bladder pain syndrome exhibit higher urinary inflammatory cytokines than healthy controls, according to earlier study. As a result, it is postulated that the COVID-19-associated cystitis can arise in the COVID-19, accompanied by de novo acute urinary symptoms, and is induced by elevated inflammatory cytokines secreted into the urinary and/or produced in the bladder.²⁰ Thus, the relation between the COVID-19 and UTIs in pregnant women could be a highly important topic that needs in-depth investigations.

Pseudomonas aeruginosa revealed good sensitivity to Ampicillin, Amikacin and Nitrofurantoin while showing low resistance against Gentamicin (75%), Cefotaxime and Ceftriaxone (70% for each antibiotic). In general, Ceftriaxone, Cefotaxime, Gentamicin and Nalidixic were the most resistant to the pathogens (Table 4). These findings are in line with a study by Rodhe, *et al.*²¹ Women who have four to five pregnancies had the highest rate of UTI, which is consistent with previous study by Malekzadegan, *et al.*²² At the ages of 24, 40, and 50, one out of every three women will require antibiotic treatment for UTIs.²³

Most bacterial isolates are susceptible to routinely-used antibiotics, such as Ceftriaxone, Cefotaxime, Gentamicin, Ciprofloxacin, and Nalidixic, which were found in 80% of the germs identified. Ampicillin, Amikacin, Erythromycin, and Nitrofurantoin sensitivity were found in the majority of bacterial isolates. As a result, rather than following global principles, the empirical antibiotic choice should be based on awareness of specific bacterial species' prevalence and antibiotic sensitivity.

Early detection of the causal agent of UTIs and determination of their drug sensitivity pattern in pregnant mothers infected with the COVID-19, according to this study, can aid in ensuring effective treatment of UTIs and preventing additional complications in the mother and fetus. Pregnant women should be given health information on the causes of UTIs and drug usage. Ampicillin, Amikacin, Erythromycin, and Nitrofurantoin are examples of antibiotics. When there are no facilities for doing

culture and susceptibility testing in their location, it might be utilized for empirical therapy of UTIs. However, it should be administered with caution to prevent the establishment of new drug resistance, particularly in patients with the COVID-19 risk factors.

Conclusion

The progression of UTIs is shown to be caused by gram-negative and gram-positive bacteria in this investigation. In pregnant women infected with the COVID-19, the most frequent pathogenic bacteria from the urinary system, *E. coli*, is the most prevalent cause of UTI. The isolated uropathogens showed high resistance to Gentamicin, Cefuroxime, Ceftriaxone and sensitive to Ampicillin and Nitrofurantoin. It is suggested to monitor the most efficient bacteriostatic medications against UTIs pathogenic bacteria, such as Ampicillin, Amikacin, Erythromycin, and Nitrofurantoin.

Abbreviations

UTI: Urinary Tract Infections; COVID-19: Coronavirus Disease 2019; WHO: World Health Organization; CLSI: Clinical and Laboratory Standards Institute.

Ethics Approval and Consent to Participate

All procedure of study was conducted with allowance and permission of the Faculty of Health Sciences, University of Misan and Maysan Health Directorate, in means of medical ethics.

Competing Interest

The authors declare that there are no significant competing financial, professional, or personal interests that might have affected the performance or presentation of the work described in this manuscript.

Availability of Data and Materials

Data and complementary findings are available when requested by the publisher.

Authors' Contribution

Single author presented in this paper.

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