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Prevalence of urinary tract infections among pregnant women in Iraq: A meta-analysis

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***Abstract*— Urinary tract infection (UTI) is the most prevalent bacterial infection in both community and hospital settings among women, especially pregnant women. It is characterized by a high incidence of treatment failure and relapses. The research aims to give an approximate percentage of the spread of the disease in various cities in Iraq, and compare it with other countries, and determine the risks of the disease and treatment for the mother and fetus. The 36 published articles have been reviewed in different regions of Iraq about pregnant women, made comparisons with other countries covered the period 2000–2023, and studied the risk factors, causative agents, and epidemiology of urinary tract infection. The results show that the rate of urinary tract infection is remarkably high in Iraq compared to other countries. UTI affects women between the ages (16-35years), *Escherichia coli* are the dominant bacteria that cause urinary tract infection, and education level has a significant effect on the prevalence of UTI.**

***Keywords*— Urinary tract infection, pregnant women**

I. Introduction

A urinary tract infection (UTI) is characterized by an inflammatory response of the urothelium upon bacterial invasion, often accompanied by the presence of both bacteria and white blood cells in the urine. Urinary tract infections (UTIs) exhibit a higher prevalence in females relative to males, mostly ascribed to recurring infections and restrictions on the administration of antimicrobial medications during pregnancy [1].

Furthermore, during pregnancy, the urinary tract experiences both physiological and anatomical alterations that promote the emergence of symptomatic UTIs in women. These changes commence around week 6 and reach their peak between weeks 22 to 24. It's noteworthy that approximately 90% of pregnant women develop urethral dilatation during this period, a condition that persists until childbirth, known as "hydronephrosis of pregnancy." These alterations encompass heightened bladder volume, diminished bladder tone, and a concurrent reduction in urethral tone, collectively fostering resulting in increased urinary stagnation and ureterovesical reflux [2]. Moreover, the normal rise in plasma volume during pregnancy leads to a reduction in urine concentration. As a result, up to 70% of pregnant women experience glycosuria, a condition that fosters the growth of bacteria in the urine. Elevated levels of urinary progestin and estrogen could potentially diminish the lower urinary tract's ability to defend from bacterial intrusion. This reduced defense may stem from a decline in urethral tone or, conceivably, by creating conditions conducive for certain bacterial strains to flourish [2,3]. All of these factors contribute to the susceptibility of pregnant women to UTIs. The primary culprits behind most UTIs are fecal organisms, *Enterobacteriaceae*, especially *E. coli* [4,5].

II. Methods

A systematic review of the literature was conducted to synthesize the prevalence of urinary tract infections among pregnant women in Iraq. The study used the search terms “UTI or Urinary Tract Infection”, “IRAQ”, “pregnant women”, “antibiotic resistance”, and “Risk factor” among several databases such as Google Scholar, Research Gate, and PubMed. All duplicated copies were then removed. All relevant records were retained for another screening, and irrelevant abstracts and titles, and studies not conducted in Iraq were removed.

III. Epidemiology of urinary tract infection in pregnancy in Iraq

Out of 36 studies, only 21 articles were selected that corresponded with all the inclusion criteria for the meta-analysis about UTI in pregnant women in Iraq, research carried out in several areas of Iraq over the years (2000-2023). As visualized in Figure 1, the findings indicate a high rate of UTI in pregnant women in Iraq in comparison to other countries.

In Baghdad, a modest decrease was observed from 32.6% in 2012 to 31.2% in 2017, Tikrit striking 72.1% in 2017. Hilla demonstrated fluctuations, with a prevalence of 48% in 2011 rised to 64.6% in 2018, and subsequently decreased to 44.8% in 2023. Samawah experienced a notable surge from 66% in 2012 to 86% in 2019. Karbala increased from 5.6% in 2010 to 48% in 2013, followed by a slight decline to 46% in 2023. Kirkuk displayed a steady

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rise from 28% in 2002 to 61% in 2020. Mosul showed a prevalence 52.6% in 2007, and Najaf exhibited a prevalence of 32.8% in 2018.

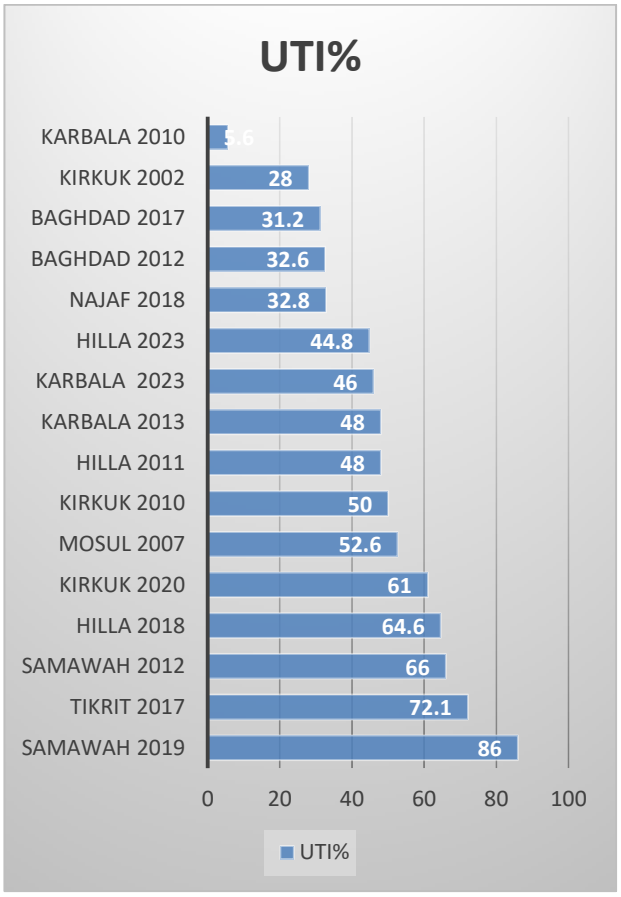

Fig 1: The prevalence of UTI among pregnant women in Iraq

In comparison with other countries, the prevalence of UTI in Iraq approximately is (48.08%) which is significantly high. In Georgia UTI in women during pregnancy was (12%) [6]. Jordan women were (20.2%) [7]. In the USA, the general occurrence of documented UTI during pregnancy was 18% in 2021. [8].

IV. Causative Agent of UTI

Six studies about pregnant women in Iraq show that *Escherichia coli* was the most predominant bacteria cause UTI, followed by Proteus mirabilis, and *Klebsiella pneumoniae* as a causative agent of UTI of gram negative bacteria among pregnant women [9-14]. *Staphylococcus aureus*, and *Streptococcus agalactiae* are the most recurrent bacteria among gram positive bacteria which cause UTI in pregnant women [11], [13], [15].

Candida albicans is the most recurrent fungi which cause UTI in pregnant women [16,17].

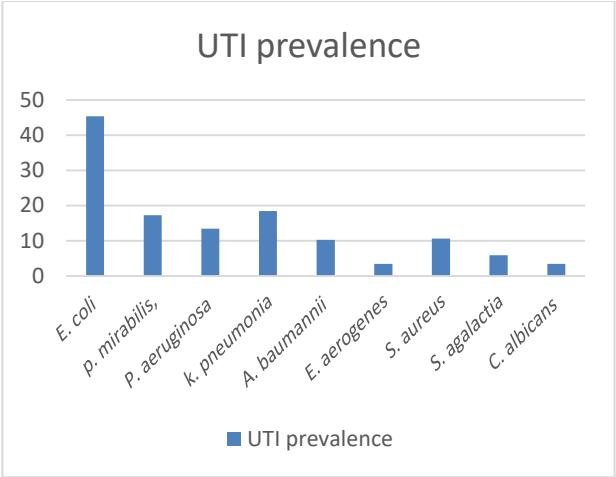

Figure 2 prevalence of causative agents of UTI in pregnant women

V. The Risks of Urinary Tract Infection on Pregnant Women and the Fetus

A. *Abortion*

Culshaw S. *et al.* [18] and Zhang C. *et al.* [19] conducted studies that showed during the bacterial infection, the body produces Interferon gamma (IFN-γ) internally, Sabeeha *et al.* [20] Conducted a study that specifically examined the levels of IFN-γ in 75 Iraqi women who experienced miscarriages and its correlation with the miscarriages. The results showed a notable rise in IFN-γ levels in the serum of all women who experienced an abortive UTI infection.

Tha'ir A *et al.* [21] assessed the association between Tumor Necrosis Factor-alpha (TNF-α) level in *P. mirabilis* UTI cases, the result showed that 62.5% of samples were positive for *P. mirabilis*. The level of TNF-α considerably was high inpatient compared with control group.

Zhang *et al.* [19] made a meta-analysis study Indicates that the serum TNF- α level is increased in patients with recurrent spontaneous miscarriages (RSM).

It enhances the production and breakdown of prostaglandin E2 (PGE2) in the chorion and decidua. This might trigger The production and discharge of PGE2 in the decidua and amniotic cells, causing the contraction of uterine smooth muscles. [22,23].

It can increase the production of prothrombin kinase Fg12 and stimulate prothrombin activation, resulting in pigment accumulation and blood clot formation in the placental blood channels [23].

It may harm the tissue lining the uterus and cells lining the umbilical vein, as well as trigger the release of particles. Consequently, this process causes thrombosis by activating factor VII, leading to malfunction of placental villi and hindering their normal growth [23].

It can trigger a Th1-type immune response and reject embryonic development [24].

TNF-a receptors in the placenta have a role in regulating sertoli cell death through intricate immunological processes [25].

B. *Asthma*

Collier *et al.* discovered that the presence of ASB, UTI, and pyelonephritis throughout pregnancy in mothers with

and without asthma was associated with a higher likelihood of asthma in their offspring up to the age of six [26].

C. *Preterm delivery*

Cunnington *et al.* presented a review identifying five publications discussing the link between UTI and premature delivery. One study demonstrated that pregnant women with a UTI had nearly double the risk of preterm birth compared to those without a UTI. Three further studies demonstrated a slight rise with point estimates ranging from 1.03 to 1.09, while one research showed no difference [27].

D. *Early-onset sepsis (EOS)*

Wright *et al.* discovered a link between early-onset sepsis in newborns, caused by antibiotic-resistant bacteria, and maternal antibiotic usage throughout pregnancy and delivery, which included antibiotics for bacteriuria (6% of prescriptions). The primary reasons for prescribing antibiotics were preterm premature rupture of membranes (PROM) and chorioamnionitis [28].

E. *Epilepsy*

Researchers discovered a little elevated likelihood of epilepsy in infants born to women who were prescribed antibiotics [29].

VI. ANTIBIOTICS USE TO TREAT URINARY TRACT INFECTION IN PREGNANT WOMEN

Pregnant women are at a heightened risk for UTIs due to variations in pathophysiology and limited treatment choices. Additionally, the infection and treatment might potentially affect both the mother and the neonate.

The emergence of multidrug-resistant bacteria complicates therapy, providing a greater risk to both the mother and fetus. This situation reduces the likelihood of prescribing effective antibiotics, makes infections challenging to eradicate, and impairs treatment success.

The selected studies show the following:

Escherichia coli have shown resistance to multiple antibiotics in numerous studies conducts in Iraq. Sameer *et al.* screened the antimicrobial sensitivity of *E. coli*, the results showed that ampicillin, doxycycline, cefotaxime, cephalexin, ceftriaxone, and ceftazidime were non effective against 31% of *E. coli* isolates, while 36% of isolates could resist piperacillin and trimethoprim/ sluphomethoxazole. Only 21%, 10% and 5% of isolates could resist cefepime, tetracycline and imipenem, respectively. High percentages of isolates could resist different antibiotics such as 73% were resistant to amikacin and gentamicin, 68% were resistant to tobramycin, 89% were resistant to ticarcillin/ clavulanic acid and nitrofurantoin, and finally 94% were gatifloxacin, levofloxacin, and sulfisoxazole resistant [30]. Ali *et al*. conducted a study which revealed that among 646 positive bacterial growth isolates, 241 were *E. coli* strains that were multidrug resistant (MDR) and 10 strains that were extensively drug resistant (XDR) [31].

Proteus mirabilis exhibited the highest resistance to ceftriaxone at 96.8%, followed by norfloxacin (82.5%), gentamicin (71.4%), ciprofloxacin (69.8%), cephalexin (52.4%), nalidixic acid (42.9%), sulfamethoxazole (39.7%), ampicillin (36.5%), and nitrofurantoin (3.2%), see [32]. *P. mirabilis* exhibited great susceptibility to ertapenem and imipenem, and high resistance to ampicillin (80.6%), aztreonam (88.9%), ceftriaxone (72.2%), and cefepime (72.2%). A further investigation demonstrated that *Proteus mirabilis* isolates displayed resistance to ampicillin (77.8%), cefepime (77.8%), and ceftriaxone (77.8%), while being 100% sensitive to imipenem, amikacin, and ertapenem [33].

Klebsiella pneumoniae exhibited complete resistance to Ampicillin and Tetracycline [13], amoxicillin [31], Chloramphenicol, Amikacin, and Imipenem were found to be effective [13] *Klebsiella pneumoniae* showed 100% sensitivity to imipenem and meropenem, 63.2% to nitrofurantoin, 56.9% to ciprofloxacin, and 54.6% to doxycycline. Other studied antibiotics demonstrated less than 50% effectiveness. The *K. pneumoniae* isolates shown significant resistance to various antibiotics: cephalothin (90.8%), ampicillin (83.3%), cefixime (82.2%), azithromycin (81.6%), amoxicillin, and nalidixic acid (78.2%) [34]. A study conducted by Hasan *et al.*, fourteen distinct antimicrobials were employed to combat *K. pneumoniae* in the investigation. The study showed that all 74 isolates were resistant to amoxicillin (100%) and 70 isolates were resistant to chloramphenicol (94.5%). High resistance rates were detected for cefotaxime, amoxiclav, and ceftriaxone (66 isolates, 89.1% and 65 isolates, 87.8% respectively). Ceftazidime also shown reduced efficiency with resistance (58 isolates, 78.3%). There was a moderate resistance rate seen for doxycycline and nitrofurantoin, with 51 isolates (68.9%) and 50 isolates (67.5%), respectively. The resistance rate was observed for Tobromycin in 44 isolates (59.4%), tetracycline in 43 isolates (58.1%), gentamycin and ciprofloxacin in 41 isolates (55.4%), and amikacin in 32 isolates (43.2%). The bacterial isolates show a high sensitivity rate to imipenem of 97.3% [35].

90% of *K. pneumoniae* isolates were multidrug-resistant (MDR) and 10% were extensively drug-resistant (XDR). The bacteria showed resistance to Amoxicillin-clavulanic acid, Cefoperazone, and Cefixime (100%), Ceftriaxone and Cefotaxime (90%), and Nitrofurantoin (70%), while being 90% sensitive to Imipenem [36].

P. aeruginosa showing resistance to amoxicillin [31] Complete resistance to Ampicillin, Cefoxitin, Tetracycline, and Trimethoprim. [13] and a susceptibility to Amikacin and Imipenem. *Pseudomonas aeruginosa* isolates exhibit high sensitivity rates to Gentamicin (100%), Ciprofloxacin (87.5%), and Tetracycline (81.25%) [37]. Measuring the effectiveness of antibiotics against *Pseudomonas aeruginosa* the results show that the bacteria was resistant to Tobramycin 53%, Cefoperazone 60%, Cefotaxime 71%, Ceftriaxone 71%, Ceftriaxone/ Cefotaxime 63%, Cefixime 100%, Nitrofurantoin 100%, Trimethoprim/ Sulfamethoxazole 87%, Ampicillin100%, Augmentin 75%, Ciprofloxacin 66% [38].

Staphylococcus aureus is 100% resistant to Penicillin and Piperacillin. [38], benzylpenicillin 100%, Erythromycin 60%, Oxacillin 60%, Clindamycin 80% [39]

Resistance to Ampicillin is 100%, and roughly 96%, 85%, 78%, 78%, and 74% for Cefotaxime, Methicillin, Norfloxacin, Cloxacillin, and Amikacin, respectively. Approximately 70% showed resistance to Trimethoprim, Tetracycline, Erythromycin, and Cephalexin. Furthermore, almost 63% of MRSA isolates showed resistance to Meropenem. Similarly, 56% were resistant to Levofloxacin and Gentamicin, while 52% were resistant to Ciprofloxacin and Rifampin [40] *S.aureus* show high resistence to Penicillin 100%, Ampicillin 95%, Amoxicillin+clavulanic acid 80%, Azithromycin & Ciprofloxacin 65% [31], and was sensitive to Cefotaxime, Ceftriaxone, Nitrofurantoin, and Augmentin 100%, Amikacin 83.3%, Gentamicin 75% [38], MRSA were sensitive to Imipenem 92.6% [40] *Streptococcus agalactia* show resistance to amoxicillin [31]

Candida albicans the studies show that Fluconazole and Ketoconazole exhibited superior efficacy against *Candida* isolates. AMP-B exhibited a broader spectrum of fungistatic activity, with 80% of the tested strains being inhibited at 3.13 µg/ml and complete inhibition achieved at 12.5 µg/ml. Fluconazole and ketoconazole both exhibited complete inhibition at a concentration of 25 µg/ml, but clotrimazole achieved 100% inhibition at 50 µg/ml. Nystatin, a polyene antibiotic with local effects, exhibited 80% inhibition at a concentration of 50 µg/ml. The results of the Minimum Fungicidal Concentration (MFC) are either equal to the Minimum Inhibitory Concentration (MIC) results or two to four times higher. [41], The isolates were fully resisted to ketoconazole and miconazole while 90.90% and 90.90% of isolates showed resistance to itraconazole and fluconazole, respectively. Lower resistance to sulfamethoxazole (81.81%) reported in the study [42] All *Candida spp* isolates were sensitive to Amphotericin B, but Fluconazole showed no effectiveness against *Candida spp* [45. Sulfamethoxazole was the most efficient antifungal against *Candida spp*. [42].

Issa SB [12] Cefixime is a successful treatment for pregnant women at any stage of their pregnancy for short-term therapy.

Imipenem exhibited the highest level of effectiveness among antibiotics tested against uropathogens [11].

Kais K. *et al.*[43] discovered Frequent presence of cephalosporin and amoxicillin-resistant bacteria in the community limits the prescription of these antibiotics to pregnant women. Amoxicillin/clavulanate and nitrofurantoin are safer options for cystitis treatment, whereas fourth-generation cephalosporins are the preferable choice for pyelonephritis.

Laith M. *et al.* [44] Conducted UTI screenings on pregnant women at different stages of pregnancy and given cefixime, a third-generation cephalosporin, to evaluate its efficacy in treating UTIs. The results show that cefixime is highly successful in treating UTIs in pregnant women during all trimesters, leading to a significant decrease in bacterial growth in urine cultures. No alterations in renal function, blood glucose, white blood cells, and hemoglobin levels were seen before and after therapy, indicating the drug's safety and acceptability. Cefixime is deemed useful for pregnant women at any stage of their pregnancy for short-term treatment.

Alhamdany [9] found Amikacin demonstrated the highest sensitivity among drugs tested against bacteria responsible for urinary tract infections. Some medicines previously used to treat urinary tract infections, like Augmentin, have shown a significant level of bacterial resistance.

Shaymaa N. [45] found *E. coli* isolates demonstrated complete susceptibility to Ampicillin, Gentamycin, and Tobramycin, *Klebsiella pneumoniae* were sensitive to Chloramphenicol, Amikacin and Impienem, *Pseudomonas aeruginosa* and *Pseudomonas stutzeri* sensitivity to Amikacin and Impienem.

VII. Risk factor of UTI

Physiological and physical changes during pregnancy, like reduced movement of the urinary system, might promote bacterial development, leading to asymptomatic bacteriuria (ASB) or urinary tract infection (UTI) [46].

Al-Rubeaan *et al.* (2013) examined 1000 diabetes patients to evaluate the occurrence and determinants of UTI. The risk factors identified were:

- female sex.
- Hypertension.
- insulin therapy.
- BMI greater than 30 kg/m2.
- nephropathy (microalbuminuria) [47],[2].

7 research carried out on pregnant women in Iraq reviewed that the age most susceptible to infection was between 16-35 years, Women in this age group are sexually active, leading to a high predicted prevalence of infection due to contact with infected individuals. [12], [16], [48-52].

The research indicated that women older than 25 years old more likely to have UTI caused by *E.coli* [52-55]. Urinary tract colonization by *E. coli* was increased in postmenopausal women due to reduced estrogen levels, leading to vaginal muscle weakness, elevated vaginal pH, and decreased vaginal flora [56].

Women with diabetes are more prone to repeated UTIs due to elevated tissue glucose levels, which create an optimal environment for the proliferation of microorganisms. This may contribute to the pathogenesis of severe pyelonephritis [57-59].

The relationship between the level of education and prevalence of UTI in pregnant women was diverse, Abdulghani M. [53], and Ameen WA [48] found that the women with high education level are more infected than low education level, counter to Riyadh D. [60], Jied SS [61], and Dhukaa'A AJ. [62] who found that low education level are more infected than high education level. They suggest that education status may impact personal hygiene practices or access to healthcare services, which in turn could influence the risk of developing UTIs during pregnancy [61], [63].

The misuse of antibiotics leads to the emergence of new strains of bacteria resistant to antibiotics [64].

PregnPregnant women who lived with a cat or a dog showed higher levels of *E. coli* in their vaginal flora and reported a higher incidence of UTI compared to pregnant women without pets. The rates of UTI were 32% for those with a cat, 27% for those with a dog, and 21% for those without any pets, suggesting a potential transmission of uropathogens between pets and pregnant women [65].

VIII. RECOMMENDATIONS

- Provide educational programs about the dangers of misuse of antibiotics, as well as regular examinations of pregnant women, especially in the first months, for the possibility of asymptomatic urinary tract infection.

- We need to establish a strict antibiotic guideline in Iraq for using antibiotics to treat urinary tract infections or any infection. This guideline should be regularly updated with the latest culture and sensitivity results to reduce the resistance of bacteria to antibiotics.

- To provide a more accurate assessment of the disease's incidence, more research on the prevalence of urinary tract infections in pregnant women in Tikrit, Mousl, and Najaf is necessary.

CONFLICT OF INTEREST

Authors declare that they have no conflict of interest.

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