RECURRENT URINARY TRACT INFECTIONS IN PREGNANCY AND ITS RELATION TO PRETERM LABOUR IN DOUR CITY

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ABSTRACT

Pregnant women easily develop urinary tract infections (UTIs) because of functional, hormonal, and anatomical changes, and also because of the location of urethral meatus which allows uropathogenic bacteria found in rectal flora access to the lower urinary tract. Many countries with higher rates of preterm birth and neonatal mortality have rates of UTI in pregnancy that exceed rates seen in more developed countries.

The aim of the study is to find out the effect of UTI on birth weight and gestational age at delivery.

Midstream urine specimens were taken from 200 pregnant in the second(T2)and third(T3)trimesters attending antenatal care departments, their ages ranging from 25-40 years old, general urine examinations were done, culture and sensitivity, and follow up of those pregnant patients till labour if it is preterm or not, and if low birth weight or not.

About 51(25.5%) were grouped as asymptomatic bacteriuria (ASB) and 149(74.5%) as symptomatic UTIs. E. coli was the predominant microorganism in both (ASB.) and symptomatic UTI (38.5%).60(30%) were primigravida, 63(31.5%) were gravida 2 and 77(38.5%) were multigravida. ASB was the most prevalent in primigravida (56.8%), while symptomatic UTI was the most prevalent in multigravida (44.3%), and this relationship was statistically significant. There were statistically non-significant relationships between maternal age with the frequency of low birth weight (LBW) and preterm labour (PTL), while the relationships between gestational hypertension, DM, and UTI are statistically significant.

It is concluded that UTI during pregnancy has a significant impact on pregnancy outcome mainly PTL and LBW. The unwanted sufferings of the pregnant mothers and their offspring could easily be prevented by early screening and prompt treatment of UTI in pregnancy.

Keywords: UTI, Pregnancy, Preterm labour, health

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INTRODUCTION

UTIs are the most common bacterial infections during pregnancy. They can lead to serious adverse maternal and neonatal outcomes. Recurrent UTI is defined as more than one UTI before or during pregnancy. A relapse is a recurrent UTI where the organism that was previously treated persists in the urinary
tract 2 weeks after completing treatment\(^1\). Severity is graded on a scale of 1-6 as follows (and also includes an anatomical component):

- **Grade 1**: cystitis, low severity.
- **Grade 2**: pyelonephritis (PN) with moderate symptoms.
- **Grade 3**: established PN with severe symptoms.
- **Grade 4**: urosepsis with systemic inflammatory response syndrome.
- **Grade 5**: urosepsis with organ dysfunction.
- **Grade 6**: urosepsis with organ failure\(^2\).

The prevalence of UTI in pregnancy is closely related to socioeconomic status, Diabetes mellitus (DM), anatomical abnormalities of the urinary tract, high parity, sickle cell disease, and age less than 15 years at first UTI.\(^{3,4}\) *E. coli* accounts for majority of UTI, as high as 80%. Klebsiella, Enterobacter, Proteus species, and enterococci infrequently cause uncomplicated cystitis and PN. Candida species are an important cause of fungal UTI, especially in immunosuppressed patients and in those with indwelling catheter\(^5\). Asymptomatic bacteriuria is marked by an absence of symptoms, and a culture from a single midstream voided urine specimen yields the same bacterial strain in any trimester in quantitative counts of more than 100,000 CFU/ml\(^6\).

**Symptomatic UTI includes:**

- **Cystitis**: an infection of the urinary bladder in which a patient may present with dysuria, frequency and lower abdominal or suprapubic pain, without fever. Pyuria may not be present\(^6\).
- **Pyelonephritis (PN)**: is an infection of the upper urinary tract in which a patient may present with fever, dysuria, tachycardia, abdominal pain, nausea and tenderness over the costovertebral angle on the side affected. It can be complicated by septic shock or renal abscess if not properly diagnosed and/or poorly treated. PN can also lead to medically-induced preterm delivery, hospital stay, anemia or respiratory dysfunction\(^7\). Patients with UTI had significantly higher rates of IUGR, preeclampsia, caesarean section, preterm delivery, and chorioamnionitis\(^8\),\(^9\). Pregnancy-related physiological changes are considered predisposing factors for UTI. These include: upper urinary tract dilatation, decreased peristalsis, smooth muscle relaxation related to relaxing effect of progesterone, mechanical obstruction from the gravid uterus, increased glomerular filtration rate, detrusor muscle relaxation and increased bladder capacity, as well as changes in the composition of urine (glycosuria-in up to 70% of pregnant female and alkaline pH)\(^10\).

**Aim:** This study aims to find out the effect of UTI on birth weight and gestational age at delivery.

**Objectives:**
1. To estimate the prevalence of UTI in Dour city pregnant.
2. To correlate UTI with preterm delivery in this population.
3. To program control and prevention measures for UTI in pregnancy and its consequent complications.

**MATERIALS AND METHODS**

Midstream urine specimens were collected in sterile containers from 200 pregnant in the second and third trimesters, ages ranging from 25-40 years old during the period from February 2019 to October 2019 and following up their labour outcomes if PTL, LBW, or not. History includes information about parity, previous UTI in non-pregnant state, systemic diseases (hypertension and DM,), and the previous use of...
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diaphragm which promotes bacterial colonization and spermicide which raises vaginal pH and is toxic to normal flora especially the lactobacilli, as well as increasing the adherence of E. coli to vaginal epithelial cells\(^{(11)}\). Symptoms include frequency, burning micturition, along with urgency and flank pain. Fever is present in limited number of patients. Urine must be processed immediately if it remains at room temperature otherwise it has to be refrigerated so as to lessen contaminants grow. Microscopical examination of urine for the presence of bacteria\(>10^5\) bacteria/ml of urine) and leukocytes\(>10 \text{ WBCs.} /\mu l\) of urine) was the first step. Hematuria and proteinuria, if present, suggest that the patient has crossed the line from uncomplicated cystitis to complicated cystitis or an upper tract infection. Urine culture is positive if bacterial count exceeds 100cfu./ml\(^{(11)}\). Culture was performed by taking urine in a sterile loop and streaking it over various media including: nutrient agar, blood agar, mannitol salt, macconkey, EMB media, with biochemical tests done such as catalase, oxidase, IMVC tests, triple sugar iron agar, and urease test for identification of bacteria. Muller Hinton agar was used, as well, for the antibiotic sensitivity testing including: Amoxiclav, Azithromycin, Nitrofurantoin, Gentamicin, Amikacin, and cephalaxin that can be used safely during pregnancy\(^{(12),(13)}\). A high protein level in urine is a warning sign. It may include kidney damage or disease or it may be a transient elevation due to infection, medication, or emotional or physical stress. Symptoms like swelling, sudden weight gain, headache and vision changes go with the differential diagnosis of preeclampsia. A positive urine test for glucose was followed by a confirmatory blood glucose test\(^{(14)}\). The lab. criteria for diagnosis of gestational diabetes mellitus(GDM) were venous plasma glucose levels of \(\geq 5.3\text{ mmol/L. after fasting and/or } \geq 8.6\text{ mmol/L. 2hr.s after an oral 75 gm glucose load}\(^{(15)}\). Preterm labour was considered if delivery was at<37 weeks, and LBW. was considered if weight<2500 gm\(^{(16)}\).

**Statistical analysis:**

The Statistical Package for Social Sciences (SPSS, version 25), and Excel, was used for data entry and analysis. Chi \((\chi^2)\) square test of association was used to compare proportions of different factors among the study groups. P value of \(\leq 0.05\) was regarded as statistically significant.

**RESULTS**

Midstream voided specimens were taken from 200 pregnant in the second and third trimesters, 51 of them were diagnosed as asymptomatic bacteriuria(ASB.) and the other 149 complain from different symptoms of UTI.

The 51 samples of ASB. patients were subdivided into: 29 primigravida, 11 gravida 2, and 11 multigravida, whereas the symptomatic UTI. patients which represent 149 cases were subdivided into: 31 primigravida, 52 gravida 2, and 66 multigravida as in table 1; Figure 1 clarifies percentages of occurrence of the causative bacterial agents; Microbiological profile of ASB. is clarified in table 2.
Table 1: Sample distribution according to UTI and gravidity

<table>
<thead>
<tr>
<th>UTI</th>
<th>Symptomatic</th>
<th></th>
<th>Asymptomatic</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Frequency</td>
<td>Percent</td>
<td>Frequency</td>
<td>Percent</td>
</tr>
<tr>
<td>Primigravida</td>
<td>31</td>
<td>20.81</td>
<td>29</td>
<td>56.86</td>
</tr>
<tr>
<td>Gravida 2</td>
<td>52</td>
<td>34.90</td>
<td>11</td>
<td>21.57</td>
</tr>
<tr>
<td>Multigravida</td>
<td>66</td>
<td>44.30</td>
<td>11</td>
<td>21.57</td>
</tr>
<tr>
<td>Total</td>
<td>149</td>
<td>100.00</td>
<td>51</td>
<td>100.00</td>
</tr>
</tbody>
</table>

X²=23.707, df=2, P value <0.05 Significant

Table 2: Sample distribution according to microbiological profile of ASB and their antibiotic resistance

<table>
<thead>
<tr>
<th>Antibiotic type</th>
<th>E. coli</th>
<th>Co.N.S.</th>
<th>Proteus spp.</th>
<th>P. aeruginosa</th>
<th>Klebsiella spp.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amoxiclav</td>
<td>8</td>
<td>22.9</td>
<td>1</td>
<td>33.3</td>
<td>1</td>
</tr>
<tr>
<td>Cephalexin</td>
<td>3</td>
<td>8.6</td>
<td>0</td>
<td>0.0</td>
<td>0</td>
</tr>
<tr>
<td>Gentamycin</td>
<td>6</td>
<td>17.1</td>
<td>0</td>
<td>0.0</td>
<td>2</td>
</tr>
<tr>
<td>Amikacin</td>
<td>7</td>
<td>20.0</td>
<td>1</td>
<td>33.3</td>
<td>3</td>
</tr>
<tr>
<td>Azithromycin</td>
<td>6</td>
<td>17.1</td>
<td>0</td>
<td>0.0</td>
<td>0</td>
</tr>
<tr>
<td>Nitrofurantoin</td>
<td>5</td>
<td>14.3</td>
<td>1</td>
<td>33.3</td>
<td>2</td>
</tr>
<tr>
<td>Total</td>
<td>35</td>
<td>100.0</td>
<td>3</td>
<td>100.0</td>
<td>8</td>
</tr>
</tbody>
</table>

X²=13.9, df=20, P value >0.05 not Significant,
Co.N.S.: coagulase negative staphylococci
Microorganism that cause different symptoms of UTI are clarified in table 3.

Table 3: Sample distribution of symptomatic UTI with their microbiological profile and antibiotic resistance

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Amoxiclav</td>
<td>13(30.95)</td>
<td>9(69.2)</td>
<td>8(40)</td>
<td>4</td>
<td>2(13.33)</td>
<td>3(15)</td>
<td>5(31.25)</td>
<td>1(50)</td>
</tr>
<tr>
<td>Cephalacin</td>
<td>1(2.4)</td>
<td>0(0)</td>
<td>0(0)</td>
<td>0(0)</td>
<td>0(0)</td>
<td>0(0)</td>
<td>0(0)</td>
<td>0(0)</td>
</tr>
<tr>
<td>Gentamycin</td>
<td>2(4.8)</td>
<td>0(0)</td>
<td>0(0)</td>
<td>1(4.4)</td>
<td>0(0)</td>
<td>1(5)</td>
<td>0(0)</td>
<td>0(0)</td>
</tr>
<tr>
<td>Amikacin</td>
<td>6(14.3)</td>
<td>2(15.4)</td>
<td>2(10)</td>
<td>2(8.7)</td>
<td>3(20)</td>
<td>8(40)</td>
<td>2(12.5)</td>
<td>0(0)</td>
</tr>
<tr>
<td>Azithromycin</td>
<td>11(26.2)</td>
<td>1(7.7)</td>
<td>4(20)</td>
<td>3(13.04)</td>
<td>2(13.33)</td>
<td>6(30)</td>
<td>1(6.25)</td>
<td>0(0)</td>
</tr>
<tr>
<td>Nitro</td>
<td>9(21.4)</td>
<td>1(7.7)</td>
<td>6(30)</td>
<td>13(56.5)</td>
<td>8(53.33)</td>
<td>2(10)</td>
<td>8(50)</td>
<td>1(50)</td>
</tr>
<tr>
<td>Total</td>
<td>42(100)</td>
<td>13(100)</td>
<td>20(100)</td>
<td>23(100)</td>
<td>15(100)</td>
<td>20(100)</td>
<td>16(100)</td>
<td>2(100)</td>
</tr>
</tbody>
</table>

X²=47.3, df=35, P value >0.05 not Significant

Table 4: Sample distribution according to mother age group and fetal complications, in terms of preterm labour (PTL).

<table>
<thead>
<tr>
<th>Age group (years)</th>
<th>PTL</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td></td>
<td>Frequency</td>
<td>Percent</td>
</tr>
<tr>
<td>25-30</td>
<td>35</td>
<td>27.6</td>
</tr>
<tr>
<td>31-35</td>
<td>42</td>
<td>33.1</td>
</tr>
<tr>
<td>36-40</td>
<td>50</td>
<td>39.4</td>
</tr>
<tr>
<td>Total</td>
<td>127</td>
<td>100.0</td>
</tr>
</tbody>
</table>

X²=5.48, df=2, P value (0.068) >0.05 not Significant

Table 5: Sample distribution according to mother age group and fetal complications, in terms of low birth weight (LBW).

<table>
<thead>
<tr>
<th>Age group (years)</th>
<th>LBW</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td></td>
<td>Frequency</td>
<td>Percent</td>
</tr>
<tr>
<td>25-30</td>
<td>35</td>
<td>27.6</td>
</tr>
<tr>
<td>31-35</td>
<td>42</td>
<td>33.1</td>
</tr>
<tr>
<td>36-40</td>
<td>50</td>
<td>39.4</td>
</tr>
<tr>
<td>Total</td>
<td>127</td>
<td>100.0</td>
</tr>
</tbody>
</table>
**Table 6:** Sample distribution according to elevated mother BP (systolic ≥130 and diastolic = 90) and mother age group.

<table>
<thead>
<tr>
<th>Age group (years)</th>
<th>Elevated BP</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td></td>
<td>Frequency</td>
<td>Percent</td>
</tr>
<tr>
<td>25-30</td>
<td>50</td>
<td>39.7</td>
</tr>
<tr>
<td>31-35</td>
<td>25</td>
<td>19.8</td>
</tr>
<tr>
<td>36-40</td>
<td>51</td>
<td>40.5</td>
</tr>
<tr>
<td>Total</td>
<td>126</td>
<td>100.0</td>
</tr>
</tbody>
</table>

\[X^2=16.86, df=2, \text{P value <0.05 Significant}\]

**Table 7:** Sample distribution according to mother age group and DM.

<table>
<thead>
<tr>
<th>Age group (years)</th>
<th>DM</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td></td>
<td>Frequency</td>
<td>Percent</td>
</tr>
<tr>
<td>25-30</td>
<td>20</td>
<td>16.8</td>
</tr>
<tr>
<td>31-35</td>
<td>39</td>
<td>32.8</td>
</tr>
<tr>
<td>36-40</td>
<td>60</td>
<td>50.4</td>
</tr>
<tr>
<td>Total</td>
<td>119</td>
<td>100.0</td>
</tr>
</tbody>
</table>

\[X^2=25.99, df=2, \text{P value <0.05 Significant}\]

**DISCUSSION**

UTI is a common clinical problem which involves urethra, bladder, and kidneys. UTI affects all age groups; women are more susceptible than men due to short urethra, absence of prostatic secretions, pregnancy and easy contamination of the urinary tract with fecal flora. Maternal UTI is independently associated with preterm delivery, preeclampsia, I.U.G.R., and CS. delivery\(^{(16)}\). Plausible explanation of increasing risk of UTI and peaking during weeks 22-24 of gestation was due to urethral dilatation, decreased tone, decreased urine concentration and increased stasis, plus hormonal changes, all these factors contribute to the increased risk with increased pregnancy duration\(^{(17)}\). The significant association between PTL and UTI is well defined, including several theories as; uterine contractions may be induced by cytokines and prostaglandins which are released by microorganisms. UTI affects PTL directly through the development of amnionitis. Furthermore, bacterial enzymes such as collagenase may weaken the fetal membranes. It was
postulated that bacterial products such as phospholipase A and C or endotoxins may stimulate prostaglandins biosynthesis by fetal membranes which initiates labour\(^{(16)}\). Many studies show that \textit{E. coli} is the most common pathogen isolated from pregnant female with UTI, one of them showed that \textit{E. coli} infection in UTI comprises about 80\%\(^{(18)}\), the study by Kareem and Rasheed showed 44\% infection with \textit{E. coli}\(^{(19)}\), while the current study shows that \textit{E. coli} is present in 38.5\% of cases. In a study by Kaul KA. et al. they found that the ability of certain uropathogenic\textit{E. coli} to adhere to uroepithelium is largely responsible for its virulence. This adherence is considered to be a prerequisite for the initiation of the disease process. The findings of increased isolation of bacterial cultures in the placentae and fetuses of the \textit{E. coli} infected animals indicate the transplacental transfer of virulent bacteria to the developing fetus. They also observed that the congenital infection in the pups of the animals that were infected with \textit{E. coli} lead to LBW, fetus and poor organ development, thereby causing an increase in the fetal death rate\(^{(20)}\). In the study by Kareem and Rasheed there were 32.8\% infection by \textit{Klebsiella pneumoniae}, 13.6\% infection by \textit{Proteus spp.} and 9.6\% infection by \textit{P. aeruginosa} in comparison to the current study which had found 13\% infection with \textit{K. pneumoniae}, 12\% infection by \textit{Proteus spp.}, and 11\% infection by \textit{P. aeruginosa}\(^{(19)}\). The study by Gilbert NM. etal. showed that \textit{S. aureus} was more predominant(29.9\%) than \textit{E. coli}(29.1\%) in ASB., while the current study shows 10\% infection with \textit{S. aureus}. Coagulase negative \textit{Staphylococci} (Co.N.S) in that study was 3\% in comparison to my study in which it was (1.5\%)\(^{(21)}\). In a study by Rizvi M. et al. they found that \textit{Enterobacteriaceae} cause 77\% of UTI. in comparison to the current study which shows 70\% infection with \textit{Enterobacteriaceae}. They found 6.4\% infection with Co.N.S., 5.9\% infection with \textit{S. aureus}, 3.4\% infection with \textit{Enterococcus spp.} in comparison to my study which shows 5.5\% enterococcal infection\(^{(22)}\).

The antibiotics used in the current study are regarded safe during pregnancy, although Nitrofurantoin which is a urinary antiseptic may increase the risk of hemolysis and G6PD deficiency in neonates. Aminoglycosides were found to have a better profile than other group of drugs but unfortunately cannot be used in pregnancy\(^{(22),(23)}\). In a study by Ali CE. et al. they found that the most frequent UTI. during pregnancy was at age of 29-32 years(34.4\%) and they found that symptomatic UTI. represent 72.4\% in comparison to the current study in which it represents 74.5\%, and that ASB. forms 27.6\% in comparison to the current study in which it forms 25.5\%\(^{(24)}\). We notice that the findings of Ali CE. etal. study are nearly similar to the findings of the current study which may be due to similar hygienic practices in both communities, similar poor measures for prevention of infection. The minor differences between studies could be due to differences in the environment, social habits of the community, the standard personal hygiene and differences in education. Untreated ASB. leads to the development of cystitis in approximately 30\% of cases, and can lead to the development of pyelonephritis in about 50\% of cases. In addition acute pyelonephritis has been associated with anemia\(^{(26)}\).

**CONCLUSION**

It is concluded that UTI. during pregnancy has a significant impact on pregnancy outcome mainly PTL. and LBW. The unwanted sufferings of the pregnant mothers and their offsprings could easily be prevented by early screening and prompt treatment of UTI in pregnancy.
ACKNOWLEDGMENT

I would like to thank God for everything. My gratitude and appreciation to patients who came to my clinic seeking for management and medical advice for their UTI. I am grateful to members of Saladdin private lab. for providing materials and equipments without which the study cannot be completed. My special thanks and gratitude to Mrs. Sarab who made the statistical analysis for the study. I would like to mention that there is no conflict of interest of my study with any researcher or institute who work in a similar field.

ETHICAL CLEARANCE

The Research Ethical Committee at scientific research by ethical approval of both environmental and health and higher education and scientific research ministries in Iraq

CONFLICT OF INTEREST

The authors declare that they have no conflict of interest.

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