

Urinary Tract Infection (UTI) as a Risk Factor of Severe Preeclampsia

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Abstract

Background: Urinary tract infection (UTI) is a very common medical complication of pregnancy. The aim of this study is to determine the incidence of UTI in preeclamptic pregnancies and its association with severity of this disease.

Methods: This cohort study was performed on 71 women with mild preeclampsia (PE), 70 women with severe PE, and 98 healthy pregnant women from October 2012 to April 2014 in the west of Iran. Mean diastolic pressure and level of proteinuria were used as indicators of disease severity. The main criteria for diagnosis of UTI was microbial count of higher than 10^4 cfu/ml.

Results: The prevalence of the UTI in severe PE patients was significantly higher than mild PE patients and non-hypertensive pregnant women. 12 out of 70 women with severe PE (17.1%) and 7 out of 98 controls (7.1%) had UTI ($P < 0.05$), also 8 out of 71 women with mild PE (11.3%) had UTI ($P > 0.05$).

Conclusions: Our data shows a significant increase in UTI in severe PE pregnancy. Thus, we can consider UTI as one of the risk factors for developing severe PE; so by screening UTI in the first visit of the pregnant women and repeating it at the second and third trimester of pregnancy we could decrease adverse effects of UTI such as severe PE in pregnant women.

Keywords: Urinary Tract Infection, preeclampsia, risk factor

1. Introduction

Preeclampsia (PE) is a common complication of pregnancy, with an incidence rate of 4–5% of all pregnancies (Lavalley et al., 2015). It is a multifactorial disorder with a familial tendency that results from complex interactions between a variety of genetic and environmental factors (Shahvaisizadeh et al., 2014). PE is characterized by new onset hypertension and proteinuria after 20th week of gestation in a previously normotensive woman, and is associated with significant maternal mortality and morbidity in the worldwide (Akolekar et al., 2011). Urinary tract infections (UTI) are one of the most common medical complications of pregnancy and characterized by the presence of significant number ($\geq 10^4$ cfu/ml) of bacteria in the urinary tract, it includes infections of the lower urinary tract (urethritis and cystitis) and the upper urinary tract (pyelonephritis). Studies show that urine culture is the gold standard method for diagnosis of UTI (Teppa et al., 2005). Because of the normal physiologic changes induced by gestation, pregnant women are especially susceptible to this infection that can result in urologic diseases and changes in kidney function which are serious threats for both mother and the fetus (Sheffield et al., 2005).

Although PE is one of the most important causes of maternal death and the major contributor of the maternal and prenatal morbidity, the mechanisms responsible for the pathogenesis of disease are unclear (Shahvaisizadeh et al., 2014).

So far, some studies on the possible relationship between UTI and increased risk of PE have been conducted and

explanations for this relationship suggest that most of them focus on indirect effects mediated by enhancing the maternal systemic inflammatory response (Easteret al., 2015; Kashanian et al., 2011). For example, chronic clinical and subclinical infections such as UTI, may increase maternal cytokine levels sufficiently to affect vascular endothelial function, and therefore prime individuals for the subsequent development of PE (Herrera et al., 2001). Considering the importance of PE and its complications, this study investigated UTI as a risk factor for increased susceptibility to developing PE in pregnant.

2. Materials and Methods

2.1 Study Design

This cohort study was conducted in the Imam Reza hospital of Kermanshah between October 2012 and April 2014. The study was performed on 70 women with average age of 29.3 ± 6.4 years old who had been diagnosed with severe PE and 71 women with average age of 29 ± 5.7 years old with mild PE. Patients who had complications such as multiple pregnancies, chronic renal and vascular disease, thromboembolism history, antibiotics or non-steroid anti inflammatory drugs use and history of smoking were excluded from the study. 98 healthy pregnant women between 36-39 weeks (27.4 ± 6.4 years of age) without hypertension and PE were used as control.

Mild PE was diagnosed according to the following criteria: a blood pressure of higher than 140/90 mmHg and proteinuria more than 300 mg/24 h or protein dipstick $\geq 1+$ on two or more midstream samples for independent 6 hours periods. Severe PE was classified if diastolic blood pressure increased to at least 110 mmHg, Proteinuria > 2000 mg/24h or protein dipstick $2+$ on ≥ 2 midstream samples during independent 6 hours periods, and also based on the presence of headache, visual disturbances, epigastric pain, oliguria (30 cc/l), elevated serum creatinine levels (0.9 mg/dl), thrombocytopenia (<100.000 mm³), and elevated aspartate and alanine transaminase levels (Shahvaisizadeh et al., 2014). Our study complies with the Declaration of Helsinki.

2.2 Culture Technique and Definitions

Mid-stream (clean-catch) specimens of urine were obtained from all patients during the period of preeclampsia and also from controls during prenatal care examination, using standard sterile technique. Urine specimens were then sent to the microbiology laboratory using sterile bottle. A loop calibrated to deliver approximately 0.001 mL was used to inoculate blood and MacConkey agar plates. All plates were incubated at 37 °C and examined daily for growth for 2 days. A positive result was defined as growth of a single urinary tract pathogen at $\geq 10^4$ CFU/mL.

2.3 Statistical Analysis

Statistical analysis was carried out using SPSS for windows 16.0 software. Chi square test was used to determine relationship between dependent and independent variable. $P < 0.05$ was considered statistically significant.

3. Results

Demographic characteristics and biochemical variables of the two groups of patients and pregnant women are shown in Table 1. Mean age and pregnancy BMI did not significantly differ between the control and experiment groups. Mean systolic and diastolic blood pressures were higher in PE groups as compared to healthy women values. The aspartate transaminase (AST), alanine transaminase (ALT), alkaline phosphatase (ALP) and proteinuria were higher in mild and severe PE. Bilirubin levels were found to be similar in three groups (Table 1).

Table 1. Clinical and laboratory findings of patients and control group

Variables	Mild PE (n=71)	Severe PE (n=70)	Healthy pregnant (n=98)	P value
Age (years)	29 ± 5.7	29.3 ± 6.4	27.4 ± 6.4	(^a <i>P</i> >0.05), (^b <i>P</i> >0.05)
Pregnancy BMI (Kg/m ²)	31.8 ± 4.8	31.1 ± 4.1	23 ± 2.9	(^a <i>P</i> <0.05), (^b <i>P</i> <0.05)
Gestational age (weeks)	30-39	30-39	36-39	(^a <i>P</i> >0.05), (^b <i>P</i> >0.05)
Systolic Blood pressure (mmHg)	140.5 ± 11.9	163.2 ± 17.6	113.2 ± 9.4	(^a <i>P</i> <0.05), (^b <i>P</i> <0.05)
Diastolic Blood pressure (mmHg)	87.5 ± 7.8	102.7 ± 9.7	74.3 ± 7.4	(^a <i>P</i> <0.05), (^b <i>P</i> <0.05)
Trace Proteinuria n (%)	28 (21.9%)	0 (0)	0 (0)	
1 ⁺ Proteinuria, n (%)	66 (51.6%)	0 (0)	0 (0)	
2 ⁺ -4 ⁺ Proteinuria, n (%)	34 (26.5%)	70 (100)	0 (0)	
AST (U/L)	28.6 ± 23.2	41.7 ± 42.5	24.2 ± 7.7	(^a <i>P</i> >0.05), (^b <i>P</i> <0.05)
ALT (U/L)	22.6 ± 29.2	32.9 ± 39	18.4 ± 6.9	(^a <i>P</i> >0.05), (^b <i>P</i> <0.05)
ALP (U/L)	336.3 ± 144.2	376.9 ± 205	218 ± 67.6	(^a <i>P</i> <0.05), (^b <i>P</i> <0.05)
Bilirubin (mg/dl)	0.53 ± 0.26	0.59 ± 0.28	0.47 ± 0.36	(^a <i>P</i> >0.05), (^b <i>P</i> <0.05)

^a*P*: Mild PE vs Healthy pregnant; ^b*P*: Severe PE vs Healthy pregnant.

Table 2 shows the prevalence of the UTI among severe and mild PE patients and healthy pregnant women. The prevalence of UTI was significantly higher in women with severe PE compared to the control group (*P*<0.05). Although UTI was shown to increase the risk for mild PE, the results, however, were not statistically significant (*P*>0.05).

Table 2. The comparison of the UTI between Severe and mild PE and controls

		Number	UTI status		p-value
			With UTI	Without UTI	
Severe preeclampsia	patients	70	12(17.1%)	58 (82.9%)	<i>P</i> < 0.05
	controls	98	7 (7.1%)	91(91.9%)	
Mild preeclampsia	patients	71	8 (11.3%)	63 (88.7%)	<i>P</i> > 0.05
	controls	98	7 (7.1%)	91(91.9%)	
Total preeclampsia	patients	141	20(14.2%)	121 (85.8%)	<i>P</i> > 0.05
	controls	98	7 (7.1%)	91(91.9%)	

4. Discussion

Preeclampsia is one of the leading causes of maternal and perinatal morbidity and mortality in developing countries. The high mortality of this disease for mother and baby emphasizes the importance of the problem. Different studies indicated various factors as risks for PE (Kashanian et al., 2011). One of the maternal complications that have been reported to associate with hypertension and PE is UTI during pregnancy (Sheffield et al., 2005).

The results of this study showed that UTI is significantly more frequent in pregnant women affected with severe PE compared to healthy pregnant women. Thus UTI can take into account to developing severe PE in pregnant women. Similar results were found in studies of Easter and colleagues and Rustveld and colleagues, they also concluded that UTI during pregnancy increases the risk of PE (Easter et al., 2015; Rustveld et al., 2008). Hill and colleagues performed a case control study and found that the frequency of UTI in women with PE were 19 percent higher than controls (Hill et al., 1986). The causal nature of this association is questionable.

In our study, range of gestational age for UTI assessment were 30-39 and 36-39 weeks in cases and control

group, respectively. Some similar studies were done irrespective of gestational age and in the others, gestational age range of cases and controls was 30 to 40 weeks (Haider et al., 2010; Emamghorashi et al., 2012). In this study the prevalence of UTI between normotensive pregnant women was 7.1%. In the study of Rajaratnam and colleagues, Masinde and colleagues, Haider and colleagues and Darzi and colleagues the prevalence of UTI were 13.2%, 17.9%, 4.3% and 2.3% respectively (Rajaratnam et al., 2014; Masinde et al., 2009; Haider et al., 2010; Darzi et al., 2011). In this study, it was found that the prevalence of UTI in pregnant women with severe PE was higher than healthy pregnant significantly. Also the prevalence of UTI was elevated in women with mild PE but it was not statistically significant. It may be due to small sample size and we suggest repeating this experiment on a larger sample size. The relationship between UTI during pregnancy and PE is consistent throughout studies performed over the last years (Conde-Agudelo et al., 2008).

Several mechanisms have been suggested to explain how maternal infection might be involved in the etiology of PE or its manifestations. Some of them express direct effects of infectious agents on the arterial walls including endothelial injury or dysfunction, acute atherosclerosis, and local inflammation that might cause relative uteroplacental ischemia (von Dadelszen et al., 2002). Furthermore, some authors have hypothesized that infection might be involved in both the initiation and progression of PE process by increasing the risk of acute uteroplacental atherosclerosis and/or its potentiating by amplifying the maternal systemic inflammatory response (Herrera et al., 2001).

Some authors argue that the association between UTI and PE may be due to confounding and not be real. For example, abnormal changes associated with chronic pyelonephritis and papillary necrosis have been observed in almost half of women with UTI during pregnancy and may cause renal dysfunction. These underlying diseases could account for the higher risk of PE among women with UTI (Mazor-Dray et al., 2009).

A study of 1533 pregnant women showed that UTI is common in pregnancy and also is a risk factor for development of pyelonephritis, low birth weight, prematurity, hypertension and PE (Minassian et al., 2013). But in a study conducted on 50 pregnant women with UTI, it was found that women with kidney problems have a 7.6 times greater risk of gestational hypertension and PE compared to controls and in the presence of natural and healthy kidneys. It is unlikely that UTI leads to PE (Loh et al., 2007). He and colleagues believe that UTI increases pyelonephritis, cystitis and kidney problems in pregnancy and patients are at risk of increased blood pressure and PE (He et al., 2013). However, in another study conducted in Croatia, it was shown that treatment of UTI in pregnant women with insulin-dependent diabetes mellitus (and not in healthy pregnant women) reduces the chance of acute pyelonephritis and PE (Drazancić et al., 1972). More data are needed to determine whether the relationship between maternal UTI and preeclampsia is causal (Darzi et al., 2011).

Considering the importance of the prevention of PE and its complications during pregnancy the researchers suggest that urine analysis and cultures be done in the first visit of pregnant women, and repeating it in the second and third Trimesters to determine whether there is an infection could prevent the serious complications such as preterm delivery, fetal growth restriction, prematurity, and elevated blood pressure during pregnancy and PE (Haider et al., 2010).

5. Conclusion

Preeclampsia is a multisystem disorder of complex origin and its prevention is not yet possible. So, prediction of preeclampsia may reduce maternal and fetal complications by proper management. Our findings suggest that women with urinary tract infection have an increased risk of developing severe PE, therefore early diagnosis followed by immediate and adequate therapy is recommended during gestation for avoiding compromising maternal and neonatal health.

Conflict of Interest and Funding

The authors have not received any funding or benefits from industry or elsewhere to conduct this study and have no conflict of interests.

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