

Research Article

## Urinary Tract Infection as a Risk Factor for Preterm Delivery : A Tertiary Hospital-Based Study

### *Infeksi Saluran Kemih (ISK) sebagai Faktor Risiko Persalinan Preterm : Penelitian Berbasis Rumah Sakit Tersier*

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#### Abstract

**Objective :** To investigate the correlation between the incidence of urinary tract infection (UTI) and preterm delivery.

**Methods :** We conducted a cohort retrospective research using patients medical records. We analysed the incidence of UTI and preterm delivery from January to December 2015, in Dr. Sardjito Hospital, Yogyakarta.

**Results :** The sample of this study covers medical records of 45 patients with preterm delivery. From total sampel, only 25 patients (55.6%) underwent urinalysis. Of these 25 patients, 15 (60%) had UTIs and all of them had preterm delivery. The result showed that 13 (86.7%) of 15 patients with bacteriuria were asymptomatic. Bacteriuria that was found in 15 subjects was not statistically significant when compared to preterm delivery indicated with relative ratio of 1,083 ( $p = 0.581 > 0.05$ ). Multivariate logistic regression analysis showed that preterm delivery were not directly related to UTI ( $p = 0.704$ ), gestational age ( $p = 0.274$ ), symptom of UTI (0.699), history of UTI ( $p = 0.999$ ), and history of coitus ( $p = 0.872$ ).

**Conclusions :** The study revealed that preterm delivery was not related to UTI. Other causes should be considered. Routine urinalysis test is recommended for pregnant women to prevent preterm delivery.

**Keywords :** bacteriuria, preterm delivery, UTIs.

#### Abstrak

**Tujuan :** Mengetahui hubungan antara infeksi saluran kemih dengan kejadian persalinan preterm.

**Metode :** Penelitian ini merupakan penelitian kohort retrospektif, menggunakan data rekam medis pasien. Analisis dilakukan terkait adanya infeksi saluran kemih pada pasien yang mengalami persalinan preterm, mulai bulan Januari sampai dengan Desember 2015, di RSUP Dr. Sardjito Yogyakarta.

**Hasil :** Sampel penelitian diambil dari data rekam medis 45 pasien dengan persalinan preterm. Dari seluruh sampel, hanya 25 pasien (55,6%) yang memiliki data pemeriksaan urinalisis. Dari 25 pasien ini, 15 (60%) dengan infeksi saluran kemih (ISK) serta persalinan prematur. Hasil urinalisis menunjukkan 13 (86,7%) dari 15 pasien adalah dengan bakteri uria asimtomatik. Bakteriuria yang ditemukan pada 15 subyek tidak bermakna secara statistik bila dibandingkan dengan terjadinya persalinan preterm, rasio relatif 1,083 ( $p = 0,581 > 0,05$ ). Analisis regresi logistic multivariate menunjukkan bahwa persalinan premature tidak terkait langsung dengan ISK ( $p$ -value = 0,704), usia gestasi ( $p$ -value = 0,274), gejala ISK (0,699), riwayat ISK ( $p = 0,999$ ), dan riwayat koitus ( $p$ -value = 0,872).

**Kesimpulan :** Penelitian menunjukkan bahwa persalinan premature tidak terbukti secara statistik memiliki hubungan dengan kejadian ISK. Perlu dipertimbangkan penyebab lain. Pemeriksaan urin alisis rutin untuk perempuan hamil dapat dipertimbangkan sebagai upaya pencegahan persalinan preterm.

**Kata kunci :** bakteri uria, ISK, persalinan preterm

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## INTRODUCTION

Preterm delivery is the leading cause of perinatal morbidity and mortality in developing countries<sup>1</sup>. Recurrent urogenital infections in pregnant women can cause preterm delivery. Yet, the correlation between asymptomatic bacteriuria and preterm delivery is still controversial<sup>1</sup>. Preterm delivery is defined as delivery before 37 weeks gestation. This term will be further divided into two, early and late preterm<sup>2</sup>. Early preterm is defined as gestational age below 33 weeks, while gestational age of 34 until 36 weeks is called late preterm. Preterm delivery is the major cause of neonatal mortality. About 1 in 10 births in the US are preterm delivery, and 40% of preterm deliveries are caused by various kinds of infections<sup>3</sup>. UTI is one of the infections that often occur in pregnant women<sup>4</sup>.

UTI is a term that indicates the presence of microorganisms in urine<sup>5</sup>. Significant bacteriuria implies pure growth of microorganisms of more than 10<sup>5</sup> colony forming units (CFU / ml) in the urine culture. Significant bacteriuria might occur without causing any clinical symptoms of UTI. This condition is called asymptomatic (covert) bacteriuria. Conversely, significant bacteriuria with clinical presentation of UTI is called significant symptomatic bacteriuria<sup>5</sup>.

A pregnant woman has a 2-10% risk of UTIs, where 20-40% cases are asymptomatic bacteriuria, 1-4% are cases of acute cystitis, even 0.5-2% is pyelonephritis. Cases of acute pyelonephritis are commonly found in the second trimester, with complications such as preterm delivery, low birth weight, preeclampsia, hypertension, kidney failure and fetal death<sup>6</sup>. Many microorganisms cause symptomatic and asymptomatic infections which then cause preterm delivery, preterm rupture of membranes, or both. The most likely mechanism is the stimulation of bacteria by prostaglandins synthesis. This can happen through the phospholipase A2 and C pathway or as a result of bacterial endotoxins entering amniotic fluid that stimulate decidual cells, which in turn produce cytokines and prostaglandins that trigger preterm delivery. The indirect pathway that does not go through substances such as interleukin 1, tumour necrosis factor and platelet-activating factor, can be found in the infected amniotic fluid<sup>7</sup>.

Meanwhile, according to Cuningham et al.

2014, it happened due to the ascending colonies of microorganisms in cervix, decidua, membrane, even up into the amnion. Lipopolysaccharide or toxins produced by the bacteria induces immune cells in the reproductive tract, production of cytokines by immune or cervix cells, decidua, and the membrane itself. It affects the myometrium and cervical effacement. Some microorganisms such as Gardnerellavaginalis, Fusobacterium, Mycoplasma hominis, and Ureaplasma urealyticum were detected more frequently than other bacteria in the amniotic fluid of pregnant women with preterm delivery. This discovery proves that pathogenic bacteria can trigger preterm delivery<sup>2</sup>.

UTI during pregnancy is a type of complicated UTIs. If left untreated, the presence of symptomatic bacteriuria potentially causes pyelonephritis, premature infants, anaemia, or pregnancy-induced hypertension. UTI that happened in the third trimester have risks such as mental retardation, slow infant growth, cerebral palsy, and fetal death<sup>5</sup>. In 2012, ACOG recommended screening for bacteriuria in the first antenatal visit. In the advanced state, the principle of management of UTIs in adult patients includes fluid intake, adequate antibiotics, and if necessary, symptomatic treatment for urine alkalinization<sup>5</sup>. This study investigates the correlation between the incidences of UTI and preterm delivery.

## METHODS

This study was an observational study with retrospective study design. This design was used to find the correlation between the incidence of UTIs and preterm delivery. The study population was all pregnant patients who had symptomatic and asymptomatic UTI at the time of preterm pregnancy, which then had preterm delivery at Dr. Sardjito Hospital, from January to December 2015. The study was done by collecting data from the medical records of these patients. Researchers recorded all the data needed to support the research. Inclusion criteria in this study were patients with preterm delivery who suffer from symptomatic and asymptomatic UTI. Exclusion criteria were patients with premature rupture of membranes and or receive induction of labour. The dependent variable was patients with preterm delivery, and the independent variable was patients with UTIs. External variables

were history of UTIs, sexual history, and history of leukorrhea.

All the data was tabulated, continued by statistical analyses (statistical significance defined as  $p < 0.05$ ). Data analysis was done using univariate, bivariate and multivariate analyses. In bivariate analysis, we assessed using Chi-square and in the last step was multivariate analysis using logistic regression analysis. This research had received an approval letter from the ethics committee to conduct basic/clinical research at Dr. Sardjito Hospital / Faculty of Medicine, Universitas Gadjah Mada, Yogyakarta.

### RESULT

The study involved 45 of 47 medical records of patients who experienced preterm delivery in Dr. Sardjito Hospital from January to December 2015.

**Table 1.** Descriptive Statistics of Subject

Variable	n	Min	Max	Mean	SD
Age	45	16	43	26.289	6.851
Gestational Age	45	25	36	30.644	3.046
Birth Weight	45	525	2860	1539.98	589.49

The mean age of the patients was  $26.29 \pm 6.85$  years; mean gestational age  $30.64 \pm 3.04$  weeks; and mean birth weight  $1539.98 \pm 589.49$  grams. Thirty-seven births were early preterm, and the remaining 8 were late preterm.

**Table 3.** Chi-square Test

Variable		Preterm Delivery		RR	CI	P-value
		Early	Late			
UTI	Yes	13 (28.9)	2 (4.4)	1.083	0.829	1.415
	No	24 (53.3)	6 (13.3)			
High-Risk Pregnancy	Yes	3 (6.7)	2 (4.4)	1.417	0.684	2.932
	No	34 (75.6)	6 (13.3)			
Symptom of UTI	Yes	4 (8.9)	1 (2.2)	0.970	0.612	1.537
	No	33 (73.3)	7 (15.6)			
History of UTI	Yes	2 (4.4)	0 (0)	0.814	0.706	0.939
	No	35 (77.8)	8 (17.8)			
History of Coitus	Yes	5 (11.1)	1 (2.2)	0.985	0.669	1.450
	No	32 (71.1)	7 (15.6)			

**Table 2.** Demographic Characteristic of Subject

Variable	Category	n	Percentage (%)
UTI	Bacteriuria	15	33.30
	Nonbacteriuria	30	66.70
Preterm Delivery	Early	37	82.20
	Late	8	17.80
High-Risk Pregnancy	Yes	12	26.70
	No	33	73.30
Symptom of UTI	Yes	5	11.10
	No	40	88.90
History of UTI	Yes	2	4.40
	No	43	95.60
History of coitus	Yes	6	13.30
	No	39	86.70

Out of 45 patients, only 25 patients (55.6%) underwent urinalysis (21 patients of early preterm delivery with gestational age less than 33 weeks, and 4 patients of late preterm delivery at gestational age 34 to 36 weeks). Of these 25 patients, 15 (60%) had UTIs and all of them had preterm delivery. Based on gestational age, there were 12 (26.7%) subjects were classified in high-risk pregnancy, and 33 (73.3%) were not. From 45 women who experienced preterm delivery, 40 subjects did not have any symptom while 5 subjects had symptoms. 95.6% subjects did not have any history of UTI.

Bacteriuria found in 13 (28.9%) early preterm delivery and 2 (4.4%) late preterm delivery was not statistically significant when compared to preterm delivery with relative ratio of 1.083 (p-value = 0.581 > 0.05). The women who had high-risk pregnancy was not statistically significant when compared with those with preterm delivery with numbers relative ratio 1.417 (p-value = 0.168 > 0.05). The number of the relative ratio indicated that those aged older than 35 years of age has the possibility to have early preterm delivery 1.4 times compared to late preterm delivery. 4 (8.9%) cases that were symptomatic founded at early preterm delivery, 1 (2.2%) cases founded at late preterm delivery with relative ratio of 0.970 (p-value = 0.890 > 0.05).

The relative ratio of 0.970 indicated that the probability of symptomatic UTI that provokes early preterm delivery and late preterm delivery was practically comparable. All subjects with a history of UTI were 2 (4.4%) cases, founded at early preterm birth had numbers relative ratio 0.814 (p-value = 0.501 > 0.05). The number showed that the possibility between those with history of UTI in early and late preterm birth was equal. The correlation between preterm delivery with a history of coitus found 5 (11.1%) cases at early preterm delivery, and 1 (2.2%) case at late preterm delivery showed relative ratio of 0.985 (p-value = 0.939 > 0.05). The relative ratio indicated that the odd from a history of coitus at early and late preterm delivery was compatible.

**Table 4.** Binary Logistic Regression Analysis

Variable	B	Sig.	OR	CI	
				Low	Upper
UTI	0.346	0.704	1.414	0.237	8.443
High-Risk Pregnancy	1.176	0.274	3.242	0.394	26.674
Symptom of UTI	-0.540	0.699	0.699	0.038	9.008
History of UTI	-20.069	0.999	0	0	-
History of Coitus	0.200	0.872	1.222	0.106	14.079

From multivariate logistic regression analysis, preterm delivery was not directly related to UTI (p = 0.704), gestational age (p-value = 0.274), symptomatic UTI (0.699), history of UTI (p-value=0.999) and history of coitus (p-value = 0.872). One study showed that patients with asymptomatic bacteriuria had a higher average of preterm delivery compared to patients with bacteriuria. About 40 to 80 per cent of pregnancy complications due to acute pyelonephritis can be prevented by treating asymptomatic bacteriuria<sup>3</sup>.

## DISCUSSION

Bacteriuria is one of the clinical problems which is quite serious in pregnancy. If left unhandled, can there are many such complications ascendent infection (pyelonephritis), the occurrence of premature rupture of membrane, preterm delivery, until infection in the neonate<sup>9</sup>. Prevalence of UTI diagnosis from the result of urinalysis reach 55.17% at this study. Another study obtained a diagnosis of UTI in reaching pregnancy 2.5%-8.7%. Maternal age is not is a risk factor significant in this study, where results it cannot be a role model due to lack of sample size<sup>10</sup>. In a previous study, reported that the incident bacteriuria was associated with preterm delivery<sup>11</sup>. In this study,

the association between age pregnancy with bacteriuria not significant meaning. Parity has a relationship with the occurrence of bacteriuria on pregnancy. Multiple patient more risk 4.78 times to get findings of bacteriuria were compared with primigravida patients<sup>10</sup>. From the results of this study, parity is not related directly with bacteriuria.

The findings of this retrospective study revealed that the average age of the patients with preterm delivery was 26.29 ± 6.85 years which means none of the samples was in high-risk pregnancy according to their age. These findings are almost comparable with the earlier study done by Patel<sup>1</sup>. The result showed that 13 (86.7%) of 15 patients with bacteriuria were asymptomatic. In one study present that women with asymptomatic bacteriuria have higher preterm delivery incidence compared with women with symptomatic bacteriuria. Around 40-80% of pregnancy complications due to acute pyelonephritis can be prevented by giving therapy in asymptomatic bacteriuria<sup>3</sup>.

From multivariate logistic regression analysis, preterm delivery was not directly related to UTI (p-value = 0.704) which is different from the

findings of a study conducted by Patel<sup>1</sup>. Other factors such as age, symptoms of UTI, history of UTI, and history of coitus also showed no significant effect on preterm delivery. Moreover, the history of UTI had a number of odds ratio of 0 which indicated that it was not identified contributing any influence on preterm delivery.

The difference of the results in these two studies was likely due to the existence of other risk factors that have a more dominant influence to cause preterm delivery in each patient and required further investigation. These other risk factors include the history of previous preterm birth as the most common cause, history of vaginal discharge, examination of vaginal swab to diagnose bacterial vaginosis, current infection in the system and other organs such as periodontal disease, lifestyle, and possible genetic involvement.

The results showed unsatisfactory results because no significant variable effect on preterm delivery was found. The number of medical records data (45 observations) within one year (2015) is not sufficiently related to cases of preterm labour. Research should be developed further by extending the time of data collection in order to find more scientific results. Furthermore, considering that this study only comprised premature delivery (early and late delivery), the involvement of normal delivery can clearly present the comparison between both normal and preterm delivery.

## CONCLUSION

This study revealed that preterm delivery was not related to UTI. It should be considered some other causes. However, the discovery of asymptomatic bacteriuria in patients with preterm delivery indicated that this might be one of the risk factors for preterm delivery. A urinalysis should be performed routinely in every pregnancy for reducing the risk factor.

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