

Meta-Analysis the Effect of Urinary Tract Infection in Pregnant Women on Prematurity and Low Birth Weight

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ABSTRACT

Background: During pregnancy there are physiological changes associated with the pregnancy process that can cause urinary tract infections caused by the enlargement of the uterus, decreased urine flow through the ureters and decreased bladder tone during pregnancy. So that healthy pregnant women become vulnerable to serious complications in the urinary tract and will have an impact on the mother and baby who will be at great risk of causing premature birth and low birth weight. This study aims to estimate the magnitude of the effect of urinary tract infections in pregnant women on premature birth and low birth weight.

Subjects and Method: This study is a systematic review and meta-analysis conducted with PRISMA flow diagrams. Search articles through journal databases including: Google Scholar, MEDLINE/PubMed, Science Direct, Spinger Link and Directory of Open Access Journal (DOAJ) by selecting articles published in 2005-2021. The keywords used were "Urinary Tract Infection Pregnancy" AND "Preterm Labor", "Urinary Tract Infection Pregnancy" AND "Low Birth Weight", "Urinary Tract Infection Pregnancy" AND "Preterm Labor" AND "Low Birth Weight" AND "adjusted Odds Ratio". Inclusion criteria included full-text articles, case-control study designs. The analysis used logistic regression with adjusted odds ratio. Eligible articles were analyzed using the Revman 5.3 application.

Results: A total of 17 articles were reviewed in this study with a case control study design. A meta-analysis of 11 articles showed that urinary tract infections in pregnant women increased the risk of preterm delivery by 2.49 times compared with pregnant women without urinary tract infections (aOR = 2.49; 95% CI = 2.04 to 3.05; $p < 0.001$), whereas 7 The article shows that urinary tract infections in pregnant women can increase the risk of increasing the risk of LBW by 1.54 times compared to pregnant women without urinary tract infections (aOR = 1.54; 95% CI = 1.24 to 1.91; $p < 0.001$).

Conclusion: Urinary tract infections increase the risk of preterm birth and low birth weight.

Keywords: urinary tract infections, prematurity, low birth weight

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BACKGROUND

Urinary tract infection (UTI) is a common health problem characterized by the

presence of bacterial infections that most commonly occur during pregnancy (Parveen et al., 2012).

In pregnancy, it is considered the most common bacterial infection with an increased risk of maternal and infant (perinatal) morbidity and mortality (Schmiedemann et al., 2007). The prevalence of urinary tract infections during pregnancy is 28.7% in European and Asian countries, 30.1% in Africa, and 41.1% in America (Platte, 2019).

Urinary tract infection is a common infection in pregnant women characterized by an inflammatory response and bacteria in the urine. Urinary tract infections generally refer to bladder infections or cystitis. Infections of the urethra are called ureteritis, pyelonephritis of the kidneys and renal pelvis, and ureteritis of the ureters (Saifuddin, 2009). This is triggered by physiological changes in the urinary tract during pregnancy that can increase the risk of urinary tract infections. These physiological changes associated with pregnancy can make healthy pregnant women vulnerable to serious complications in the urinary tract (Vasudevan, 2014).

Physiological changes include uterine enlargement, decreased urine flow through the ureters (urinary peristalsis) and decreased bladder tone which causes an increase in plasma volume that triggers bacterial growth (Abanto et al., 2020).

The risk of urinary tract infections is higher in the third trimester compared to the first and second trimesters. In addition, urinary tract infections during pregnancy contribute significantly to maternal and perinatal morbidities such as abortion, small birth size, maternal anemia, hypertension, preterm labor, phlebitis, thrombosis and chronic pyelonephritis (Lawani et al., 2015; Parveen et al., 2012). The incidence of urinary tract infections is more common in women than men because the female urethra is shorter, close to the anus and the vagina (Mittal and Wing, 2005).

Based on the results of research which states that the population of mothers who experience urinary tract infections during pregnancy has a direct strong influence on negative birth outcomes such as premature birth and low birth weight (Wague et al., 2020). This is also reinforced by the results of other studies which state that women who have high levels of urinary tract infections are more at risk of developing prenatal and postnatal infections (Gayathri et al., 2018).

The incidence of urinary tract infections has a high risk of premature birth and low birth weight which can have a detrimental impact on infants or children who are born more at risk of developing hyaline membrane disease, asphyxia, intracranial bleeding, neurological disorders, hypothermia, metabolic disorders and a tendency to infection. neonates. While long-term complications include mental retardation, sensory disturbances such as hearing loss, vision and retinal disorders ROP (retinopathy of prematurity) as well as additional economic costs for the family for the care of premature babies and low birth weight babies (Nugroho et al. , 2012).

Premature birth and low birth weight caused by exposure to urinary tract infection in this case urinary tract infection is an important determinant of preterm labor and low birth weight (Shubhada et al., 2013).

There are studies that state that women who are exposed to urinary tract infections during pregnancy give birth to more children with low birth weight by 4.09 times compared to women who do not get urinary tract infections during pregnancy (Rafati et al., 2008).

Based on research data regarding the impact of urinary tract infections experienced by pregnant women, and proper handling and treatment is needed for premature birth and low birth weight (Wague et al., 2020). So researchers are

interested in studying the effect of urinary tract infections in pregnant women on premature birth and low birth weight (LBW). The data obtained will be analyzed using a systematic review and meta-analysis in an effort to obtain comprehensive results by synthesizing the results of primary studies involving the effect of urinary tract infections in pregnant women on premature birth and low birth weight (LBW). The results will be analyzed using RevMan 5.3 software which has been previously synthesized to reduce bias.

SUBJECTS AND METHOD

1. Study Design

This was a systematic review and meta analysis. Article searches were carried out using journal databases including: Google Scholar, MEDLINE/PubMed, Science Direct, Spinger Link, and Directory of Open Access Journal (DOAJ), articles in vulnerable years 2005-2021 with the keywords “Urinary Tract Infection Pregnancy” AND “Low Birth Weight”, “Urinary Tract Infection Pregnancy” AND “Preterm Labor” AND “Low Birth Weight” AND “adjusted Odd Ratio”. The data were screened using the PRISMA flow chart.

2. Inclusion Criteria

This study has inclusion criteria, including: Full paper article with Case-Control study design, the analysis used logistic regression with adjusted Odds Ratio. Subjects in the study were pregnant women who had urinary tract infections and the outcome was premature birth and low birth weight.

3. Exclusion Criteria

This study has exclusion criteria, including: Articles published other than English, Studies conducted using a Randomized Control Study (RCT), protocol studies, and pilot studies, Paid or inaccessible articles, Not multivariate analysis studies, and Articles with the condition of pregnant women

with multiple pregnancies and comorbidities such as stress disease, mental illness, severe depression, heart disease, pre-eclampsia, gestational diabetes, and urinary tract infections before pregnancy.

4. Operational Definition of Variables

The formulation of the research problem was carried out by considering the eligibility criteria defined using the PICO, namely Population: pregnant women, Intervention: urinary tract infection, Comparison: no urinary tract infection and Outcome: premature birth and LBW.

Urinary tract infections in pregnant women are pregnant women experiencing urinary tract infections caused by physiological changes in the urinary tract that trigger bacterial growth and have an impact on infection.

Premature birth is the birth of a baby spontaneously or by cesarean section at a gestational age of <37 weeks from the calculation of the First Menstrual Last Menstruation (LMP).

Low Birth Weight (LBW) is a newborn baby weighing <2500 grams regardless of the mother's gestational age at delivery.

5. Instrument

Assessment of the quality of research articles is carried out using the Critical Appraisal Checklist for Case Control (CEBM, 2005).

6. Data Analysis

Data analysis in this study used the Review Manager application (RevMan 5.3). The data were analyzed based on variations between studies by determining the use of the fixed effects analysis model. In this study, I^2 was used to quantify the dispersion. The results of the data analysis are in the form of the effect size value of the heterogeneity of the study which later the results of the analyzed data are interpreted in the form of forest plots and funnel plots.

RESULTS

Research from primary studies related to the effect of urinary tract infections in pregnant women on preterm birth and low birth weight contained 17 articles from 4 continents, namely, 1 study from the North American continent, 1 from the South American continent, 8 from the African continent and 7 from the African continent. Asian continent.

The article search was carried out using a database based on the PRISMA flow diagram, which can be seen in Figure 1. The

study quality assessment was carried out qualitatively and quantitatively. Assessment of research quality using the Critical Appraisal Checklist for Case Control Study (CEBM, 2005). can be seen in Table 1. Each of the 11 questions was answered with a choice of answers: if Yes, a value of 1 and No, a value of 0. After the study quality assessment was carried out, a total of 17 articles included in the quantitative synthesis process of the meta-analysis were analyzed using RevMan 5.3.

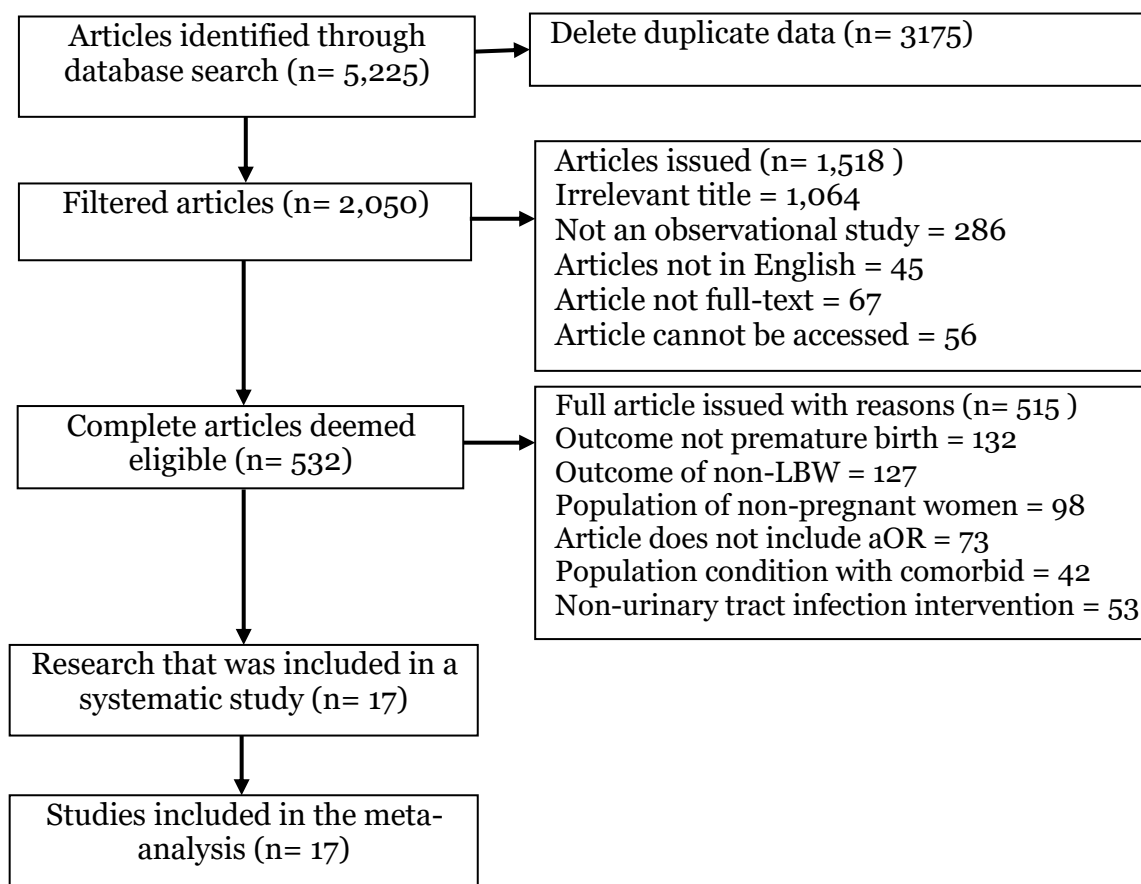


Figure 1. PRISMA diagram flow

Table 1. Assessment of the Quality of Research on Urinary Tract Infections in Pregnant Women on Premature Birth

No	Question	Alijahan et al. (2014)	Dabbagh et al. (2006)	Dahman (2020)	Egbe et al. (2020)	Gejo et al. (2021)	Mahapula et al. (2016)	Rugaimuk am et al. (2017)	Suresh-babu et al. (2021)	Temu et al. (2016)	Valipour et al. (2020)	Wakeyo et al. (2020)
		Skor	Skor	Skor	Skor	Skor	Skor	Skor	Skor	Skor	Skor	Skor
1	Does the research address clearly focused questions/problems?	1	1	1	1	1	1	1	1	1	1	1
2	Is the research method (study design) appropriate to answer the research question?	1	1	1	1	1	1	1	1	1	1	1
3	Are there enough subjects (employees, teams, divisions, organizations) in the research to establish that the research did not occur by chance?	1	1	1	1	0	1	1	1	1	1	1
4	Was the selection of cases and controls based on external, objective and validated criteria?	1	1	1	1	1	1	1	1	1	1	1
5	Were the two groups comparable at the start of the study?	0	0	0	1	0	1	1	1	1	0	0
6	Were objective and unbiased outcome criteria used?	0	0	0	0	0	0	0	0	0	0	0
7	Is there data dredging?	0	0	0	0	0	0	0	0	0	0	0
8	Were objective and validated measurement methods used to measure results? If not, were results assessed by someone who was not aware of the group assignments (eg whether the rater was blind).	1	1	1	1	1	1	1	1	1	1	1
9	Are effect sizes practically relevant?	1	1	1	1	1	1	1	1	1	1	1
10	How precise is the estimate of the effect? Is the confidence interval given?	1	1	1	1	1	1	1	1	1	1	1
11	Could there be confounding factors that have not been taken into account?	1	1	1	1	1	1	1	1	1	1	1
12	Can the results be applied to your organization?	1	1	1	1	1	1	1	1	1	1	1
Total Score		9	9	9	10	9	10	10	10	10	9	9

Table 2. Assessment of the Quality of Research on Urinary Tract Infections in Pregnant Women Against LBW

No	Question	Alemu et al (2018)	Arreola et al (2005)	Egbe et al (2020)	Jacob et al (2021)	Mirzaharimi et al (2013)	Moise et al (2017)	Erica et al (2019)
1	Does the research address clearly focused questions/problems?	1	1	1	1	1	1	1
2	Is the research method (study design) appropriate to answer the research question?	1	1	1	1	1	1	1
3	Are there enough subjects (employees, teams, divisions, organizations) in the research to establish that the research did not occur by chance?	1	1	1	1	0	1	1
4	Was the selection of cases and controls based on external, objective and validated criteria?	1	1	1	1	1	1	1
5	Were the two groups comparable at the start of the study?	0	0	1	1	0	1	1
6	Were objective and unbiased outcome criteria used?	0	0	0	0	0	0	0
7	Is there data dredging?	0	0	0	0	0	0	0
8	Were objective and validated measurement methods used to measure results? If not, were results assessed by someone who was not aware of the group assignments (eg whether the rater was blind).	1	1	1	1	1	1	1
9	Are effect sizes practically relevant?	1	1	1	1	1	1	1
10	How precise is the estimate of the effect? Is the confidence interval given?	1	1	1	1	1	1	1
11	Could there be confounding factors that have not been taken into account?	1	1	1	1	1	1	1
12	Can the results be applied to your organization?	1	1	1	1	1	1	1
	Total Score	9	9	10	10	9	10	10

1. Effect of urinary tract infection in pregnant women on premature birth

a. Forest plot of urinary tract infection in pregnant women against preterm birth

Interpretation of the results of the meta-analysis process can be seen through the forest plot. Figure 2 shows as many as 11 articles reporting that urinary tract infections in pregnant women can increase the incidence of preterm birth compared to pregnant women without urinary tract infections. Meanwhile, there was homogeneity between studies ($I^2 = 39\%$; $p < 0.001$). Thus, the Fixed Effect Model is used to analyze the data in the forest plot. Urinary tract infection in pregnant women has a risk of 2.49 times increasing the incidence of preterm birth compared to pregnant women without urinary tract infection and statistically significant ($aOR = 2.49$; $95\% CI = 2.04$ to 3.05 ; $p < 0.001$).

b. Funnel plot of urinary tract infection in pregnant women against preterm birth

A funnel plot is a plot that represents the approximate size of the effect of each study on the estimate of its accuracy, which is usually the standard error. Figure 3 funnel plot of urinary tract infections in pregnant women against preterm births shows that

Study or Subgroup	log[Odds Ratio]	SE	Weight	Odds Ratio IV, Fixed, 95% CI
Alijahan 2014	0.5878	0.2999	11.7%	1.80 [1.00, 3.24]
Dabbagh 2006	1.0225	0.2275	20.3%	2.78 [1.78, 4.34]
Dahman 2020	0.4068	0.2579	15.8%	1.50 [0.91, 2.49]
Egbe 2020	1.5261	0.4511	5.2%	4.60 [1.90, 11.14]
Gejo 2021	-0.8916	1.2003	0.7%	0.41 [0.04, 4.31]
Mahapula 2016	0.9933	0.4137	6.1%	2.70 [1.20, 6.07]
Rugaimukam 2017	1.3083	0.289	12.6%	3.70 [2.10, 6.52]
Sureshbabu 2021	1.3002	0.4954	4.3%	3.67 [1.39, 9.69]
Temu 2016	0.6206	0.2634	15.2%	1.86 [1.11, 3.12]
Valipour 2020	1.6864	0.4489	5.2%	5.40 [2.24, 13.02]
Wakeyo 2020	1.2809	0.6049	2.9%	3.60 [1.10, 11.78]
Total (95% CI)			100.0%	2.49 [2.04, 3.05]
Heterogeneity: $Chi^2 = 16.46$, $df = 10$ ($P = 0.09$); $I^2 = 39\%$				
Test for overall effect: $Z = 8.91$ ($P < 0.00001$)				

there is a publication bias which is characterized by asymmetric plots.

2. Effect of urinary tract infection in pregnant women on LBW

a. Forest Plot of urinary tract infection in pregnant women against LBW

Interpretation of the results of the meta-analysis process can be seen through the forest plot. Figure 4 shows as many as 7 articles reporting that urinary tract infections in pregnant women can increase the incidence of low birth weight (LBW) compared to other interventions or pregnant women without urinary tract infections. Meanwhile, there was homogeneity between studies ($I^2 = 15\%$; $p < 0.001$). Thus, the Fixed Effect Model is used to analyze the data in the forest plot. Urinary tract infections in pregnant women have a risk of 1.54 times increasing the incidence of Low Birth Weight (LBW) compared to pregnant women without urinary tract infections and statistically significant.

b. Funnel Plot of urinary tract infection in pregnant women against LBW

Figure 5 funnel plot of urinary tract infections in pregnant women against LBW, shows that there is no publication bias which is indicated by the symmetry of the plot.

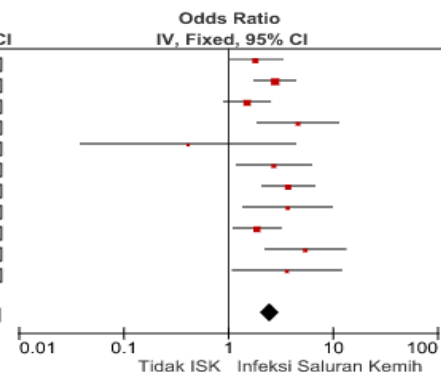


Figure 2. Forest plot of urinary tract infections in pregnant women against preterm birth

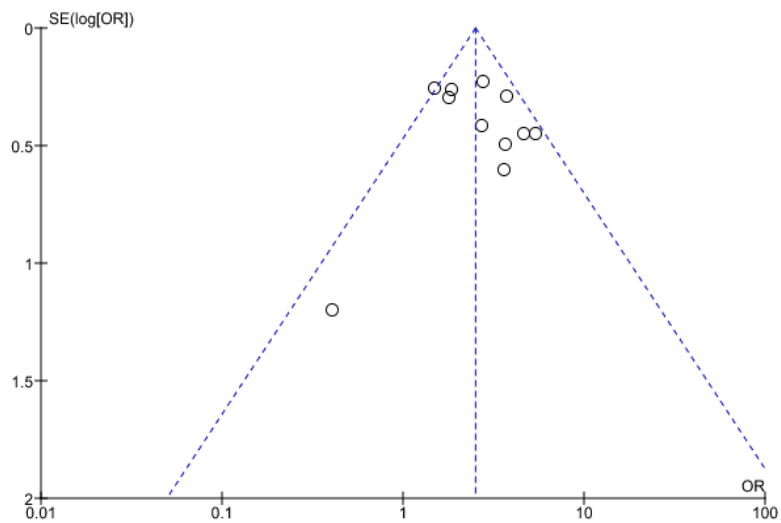


Figure 3. Funnel plot of urinary tract infections in pregnant women against premature birth

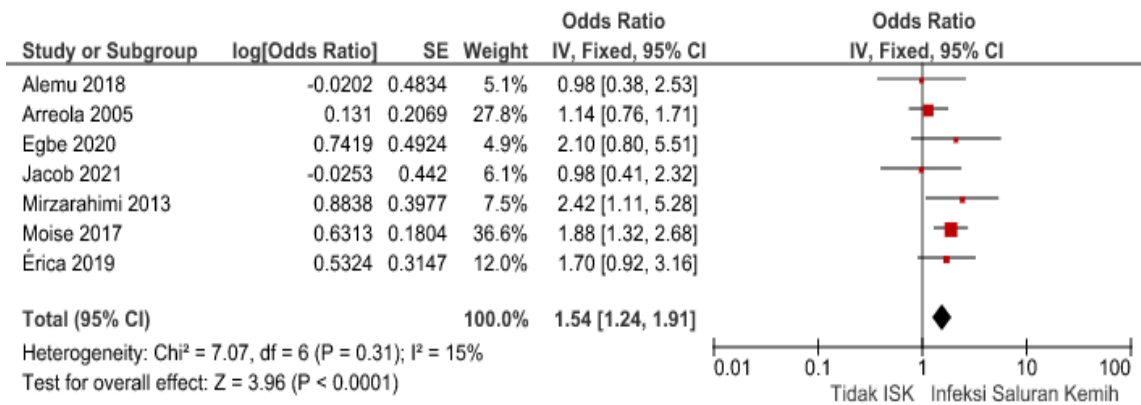


Figure 4. Forest plot of urinary tract infections in pregnant women against LBW

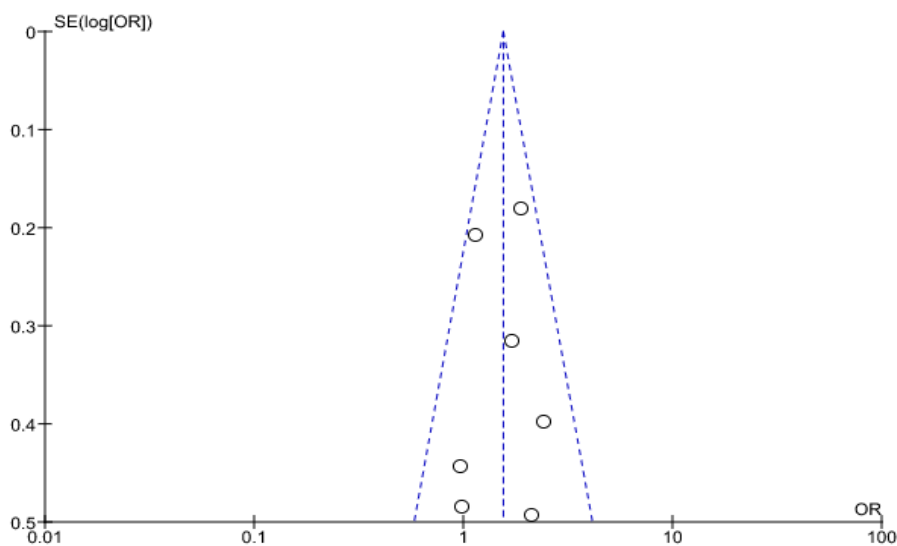


Figure 5. Funnel plot of urinary tract infection in pregnant women against LBW

DISCUSSION

This study is a systematic study and meta-analysis with the theme of the effect of urinary tract infection in pregnant women on premature birth and low birth weight (LBW). The independent variable was urinary tract infection. The dependent variables studied were premature birth and low birth weight. The results of primary studies carried out with systematic reviews and meta-analyses indicate epidemiological study designs with larger samples, different demographic characteristics in both developed and developing countries, thus providing a basis for concluding that urinary tract infections in pregnant women affect preterm birth and delivery. LBW.

Premature birth is one of the direct causes of risk factors for neonatal death, especially because it is associated with infectious diseases, one of which is urinary tract infection. It is associated with medical conditions that impair placental circulation and efficiency, fetal development or growth or the general health and nutrition of the mother (Behrman et al., 2007).

The large number of case-control studies with suitable case and control samples and laboratory results contained in maternal medical records related to urinary tract infections provide the basis for concluding that urinary tract infection is a significant risk factor for preterm birth, so the results of this study indicate that the relationship between Urinary tract infections in pregnant women with preterm birth appear to apply to women of various nationalities, cultures and social classes with few exceptions. Urinary tract infections if treated or untreated will have the potential for serious and life-threatening sequelae (Minassian et al., 2013). So that this can reduce the utilization of prenatal care to detect infection and the availability of timely and limited medical interventions due to the inadequate

number of health care providers thereby reducing adherence to treatment which contributes to preterm labor associated with urinary tract infections. Urinary tract infections are also associated with behaviors such as sexual activity, smoking, and lack of personal hygiene (Eniola et al., 2014).

This study also supports previous research that pregnant women with urinary tract infections have a risk of giving birth to premature babies 1,501 times greater than those without urinary tract infections (AOR= 1.50; 95% CI = 0.91 - 2.49) (Dahman H, 2020) . This is in line with another study which stated that pregnant women who had urinary tract infections had a 3.23 times chance of experiencing preterm labor than those who did not have a history of UTI during pregnancy (OR= 3.23; 95% CI 1.25-8.33) (Shahira et al., 2007)

This study is also in line with other studies which state that pregnant women who have a higher frequency of urinary tract infections occur in the third trimester compared to the first and second trimesters. This is due to the effect of greater uterine pressure on the ureter during the third trimester, as well as the increased smooth muscle relaxation effect of pressure on the bladder from the descending presenting part which can cause urinary stasis which will encourage the proliferation of bacteria (Okonko et al., 2010). .

And urinary tract infections in pregnancy can have an impact on the mother and fetus such as pre-eclampsia toxicemia (PET), low birth weight (LBW), anemia, intrauterine growth retardation (IUGR), preterm labor (PTL), postpartum endometritis and premature rupture of membranes. (KPD) (Jain et al., 2013).

Urinary tract infections can cause low birth weight due to certain bacterial products that stimulate local cytokinin product-

ion that can cause premature uterine contractions or local inflammatory responses due to rupture of membranes (PROM) in this case related to antepartum bleeding, preterm birth and failure fetal growth, and can cause other complications such as pre-eclampsia. Abnormalities in the placenta such as inappropriate surface area, growth abnormalities, infarction and others can interfere with its function in supporting intrauterine fetal life (Mahayana et al., 2015). PROM also causes oligo-hydramnios which will compress the umbilical cord resulting in asphyxia and hypoxia in the fetus and reduce nutrition to the fetus and disrupt fetal growth (Cunningham et al., 2010).

This is in line with other studies which state that mothers who have urinary tract infections have a 1.4 times chance of giving birth to babies with low birth weight compared to pregnant women who are not exposed to UTI (OR= 1.4; 95% CI 1.2-1.6) (Delzell et al., 2000).

Mothers who develop urinary tract infections during pregnancy exhibit adverse perinatal outcomes as well as a higher cumulative incidence of postnatal care related to long-term infections in their offspring that can result in death. It is also influenced by age, parity, education, and living environment, mothers who live in disadvantaged areas are at higher risk of experiencing low birth weight. As well as the presence of socioeconomic factors that can directly affect fetal development, but as an intermediary to increase the risk of adverse events at the time the fetus is born, such as maternal nutrition, maternal physical activity, poor access to quality prenatal care, and maternal psychosocial behavior (Abu-Saad and Fraser, 2010). 2010).

The results of another similar study stated that there was an effect of urinary tract infection in pregnant women on the

incidence of LBW which had 1.5 times the chance compared to mothers who did not have urinary tract infections (aOR= 1.5; 95% CI= 0.47 to 4.50). The process of fetal growth and development can be affected by urinary tract infections which result in impaired reproductive system so that it affects birth weight (Bobak et al., 2005).

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AUTHORS' CONTRIBUTION

Rizqi Amalia Wulandari is the main researcher who chooses the topic, searches and collects research data. Uki Retno Budi-hastuti and Bhisma Murti analyzed data and reviewed research documents.

CONFLICT OF INTEREST

There is no conflict of interest.

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