

Effect of Urinary Tract Infection on Premature Birth: A Meta Analysis

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ABSTRACT

Background: Neonatal mortality in the world is mostly caused by premature birth (43%), and in Indonesia the biggest cause of neonatal death is premature birth (45%). One of the causes of pregnant women experiencing premature labor, namely urinary tract infections due to changes in the urinary tract system during pregnancy. This study aims to analyze the primary study of the effect of urinary tract infections in pregnant women on preterm delivery with a meta-analysis.

Subjects and Method: This study is a meta-analysis with the following PICO, population: pregnant women. Intervention: Having a urinary tract infection. Comparison: No urinary tract infection. Outcome: Premature delivery. The articles used in this study were obtained from three databases, namely Google Scholar, Pubmed, and Science Direct. Keywords to search for articles ("urinary tract infection" AND "preterm labor" OR "premature birth" OR "premature labor"). The included article is full text in English with a case-control study design from 2006 to 2022 and reports the adjusted odds ratio in a multivariate analysis. The selection of articles is done by using PRISMA flow diagram. Articles were analyzed using the Review Manager 5.3 aplikasi application.

Results: A total of 10 case-control studies from Iran, Iraq, India, Tanzania, Ethiopia, and Peru were selected for the meta-analysis. The data collected showed that pregnant women with urinary tract infections increased the occurrence of preterm labor by 2.19 times compared to pregnant women who did not experience urinary tract infections (aOR= 2.19; 95% CI= 1.80 to 2.66; p<0.001).

Conclusion: Urinary tract infection during pregnancy increases the incidence of preterm labor.

Keywords: urinary tract infection, premature delivery, meta-analysis.

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BACKGROUND

Neonatal deaths in the world are mostly caused by premature birth (43%), asphyxia neonatorum (30%), followed by sepsis (15%), congenital abnormalities (9%), and diarrhea (3%). And in Indonesia the biggest cause of neonatal death is premature birth (45%), followed by neonatal asphyxia (25%), sepsis (20%), congenital abnormalities (6%),

and diarrhea (4%) (IDHS, 2017).

Premature labor occurs at a gestational age of more than 20 weeks and before 37 weeks (American College of Obstetricians and Gynecologists, 2016). Most premature births occur in India 3,519,100 million premature births, China 1,172,300 million premature births, Nigeria 773,600 million premature births, Pakistan 748,100 million

premature births, Indonesia 675,700 million premature births, United States 517,400 million premature births, Bangladesh 424,100 million premature births, Philippines 348,900 million premature births, Democratic Congo 341,400 million premature births, and Brazil 279,300 million premature births (WHO, 2018).

In Indonesia, the highest neonatal mortality rate caused by premature birth is found in North Maluku Province at 37/1,000 live births, followed by West Papua at 35/1,000 live births and West Nusa Tenggara at 33/1,000 live births. Meanwhile, the lowest neonatal mortality rate caused by premature birth is in East Kalimantan Province at 12/1,000 live births (Risksdas, 2013).

The causes of pregnant women experiencing premature labor include multiple pregnancies, infections and chronic conditions such as diabetes and high blood pressure (WHO, 2018). Approximately 39.6% of preterm deliveries are due to infection i.e., urinary tract infection (Masteryanto et al., 2015).

During pregnancy, there are several changes in the urinary tract system, including anatomical changes, namely dilatation of the ureter and collecting system as well as physiology, namely residual urine and disturbances in the urine output process due to peristalsis and muscle tone disorders due to hormonal changes which are predisposing factors causing urinary tract infection (Cunningham et al., 2013).

The purpose of this study was to determine the effect of urinary tract infection in pregnant women on preterm labor using a meta-analysis study.

SUBJECTS AND METHOD

1. Study Design

This study uses a meta-analysis. The search for articles in this study was conducted

using electronic databases such as Google Scholar, PubMed, and Science Direct. The articles used were published from 2006-2022. The keywords used to retrieve the articles were: (“urinary tract infection” AND “preterm birth” OR “premature labor” OR “preterm labor”). The results of the search for articles in this study are listed in the PRISMA diagram and analyzed using the Review Manager 5.3 application.

2. Steps of Meta-Analysis

Meta-analysis is carried out through 5 steps as follows:

- 1) Formulate research questions in PICO (Population, Intervention, Comparison, and Outcome).
- 2) Searching for primary study articles from various databases including Google Scholar, PubMed, and Science Direct.
- 3) Perform screening and conduct critical quality primary studies.
- 4) Perform data extraction and enter the estimated effect of each primary study into the RevMan 5.3 application.
- 5) Interpret the results and draw conclusions.

The assessment of critical criteria is carried out by 2 independents using the Critical Appraisal Skills Program published by the 2018 Critical Appraisal Skills Program which consists of 12 questions. The questions are answered by giving a score. A score of 0 for answers was not carried out in the primary study, and a score of 1 for answers if done. The primary study is carried out if the total is at least 10. Then it is entered into the RevMan 5.3 application.

3. Inclusion Criteria

Full paper article with case control study, multivariate analysis with Adjusted Odds Ratio (aOR) to measure the estimated effect, research subjects are pregnant women, research intervention is experiencing urinary tract infection comparison or comparison is not experiencing urinary tract infection,

premature delivery outcome.

4. Exclusion Criteria

Articles published other than English, articles prior to 2006 and previous studies using meta-analyses.

5. Operational Definition of Variable

In formulating research problems PICO is used. The population was pregnant women, the research intervention was experiencing urinary tract infection.

Urinary tract infection is a condition when the organs including the kidneys, ureters, urethra or bladder, including the urinary system, become infected.

Premature labor is the birth of a baby earlier, i.e. before 37 weeks of gestation.

6. Instrument

Quality assessment in this study uses the

Critical Appraisal Checklist for Case Control published by the Critical Appraisal Skills Program.

7. Data Analysis

The articles in this study were collected using PRISMA diagrams and analyzed using the Review Manager 5.3 application by calculating effect sizes and heterogeneity to determine the combined research model and form the final results of the meta-analysis.

RESULTS

The primary study on the effect of urinary tract infections in pregnant women on preterm labor consisted of 10 articles, 5 studies from the Asian continent, 4 studies from Africa, and 1 study from South America

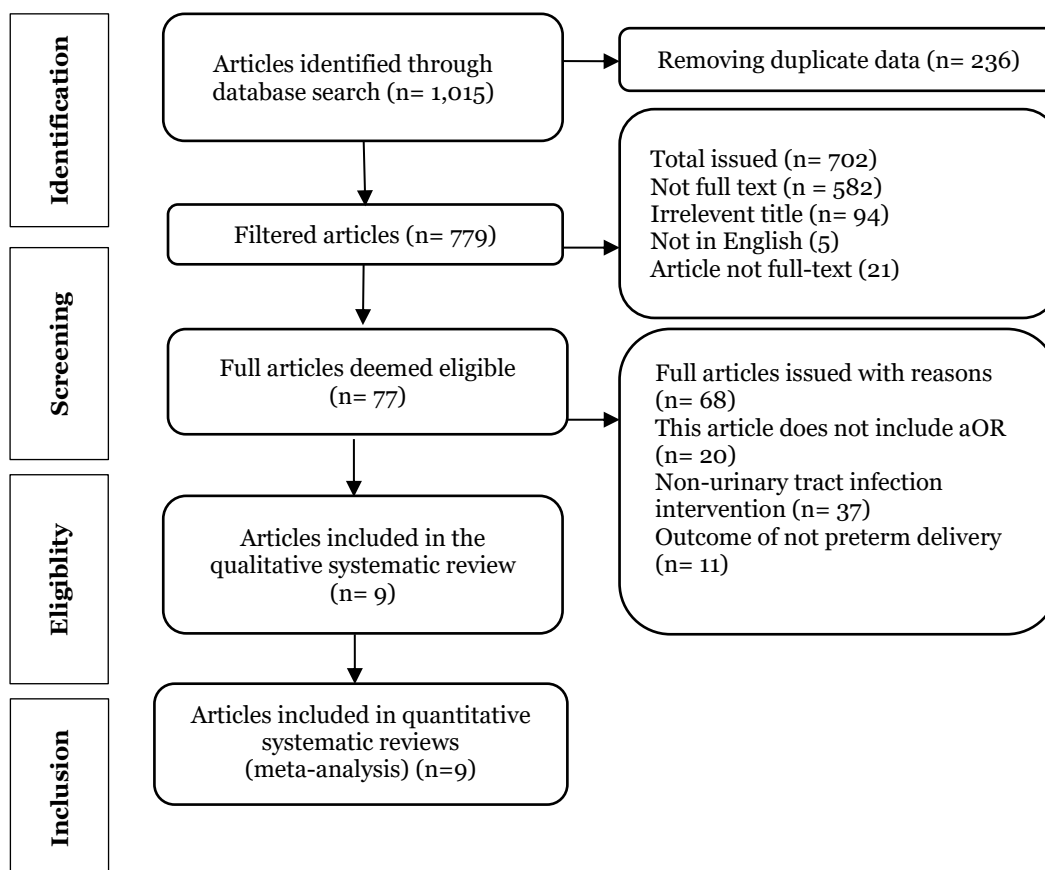


Figure 1. PRISMA Flowchart



Figure 2. Map of Research Locations

A total of 1,015 articles were identified through the electronic database. After removing duplication, 779 articles were screened. Of these, 77 articles were assessed for eligibility. The following reasons are given for full-text articles that meet the exclusion criteria:

1. The article reports only the crude odd ratio (OR) resulting from the bivariate analysis.
2. The effect size used is aRR/aHR, not aOR.
3. The article reports the outcome other than urinary tract infection in pregnant women on preterm labor.

A total of 10 articles that met the quality assessment were included in the quantitative synthesis using Meta-Analysis.

Research Quality Assessment

Critical Appraisal Checklist for Case Control Study published by Critical Appraisal Skills Program.

This assessment criteria consists of twelve criteria, with each measure given a score of 1 = if you answer yes, 0 = if you answer no. The following are the assessment criteria from the Case Control Study published by the Critical Appraisal Skills Program, including:

1. Are the test results valid?

2. Does this objective clearly address the research focus/problem?
3. Is the case control research method suitable to answer the research question?
4. Are the cases representative of the designated population?
5. Are the selected controls appropriate and acceptable?
6. Is this research instrument valid and reliable?
7. Is there any confounding of multiple pregnancies?
8. Are the results applicable to your research?
9. Is the estimated effect correct?
10. Is there a degree of confidence interval?
11. Are the results applicable to the designated population?
12. Are the results of this study consistent with other available evidence?

The next step is to calculate the overall effect of combining the data. Data analysis was carried out using Review Manager (RevMan) 5.3 software released by the Cochrane Collaboration.

Table 1 shows the assessment of study quality using the Case Control Study Checklist published by the Critical Appraisal Skills Program.

Table 1. Assessment of the quality of case control research studies

No	Questions	Al Dabbagh et al. (2006)	Ali jahan et al. (2014)	Bojorqu ez et al. (2020)	D'souza et al. (2015)	Fetene et al. (2022)	Mahapula et al. (2016)	Soun darajan et al. (2016)	Suresh- babu et al. (2019)	Temu et al. (2016)	Wakeyo et al. (2020)
1	Are the test results valid?	1	1	1	1	1	1	1	1	1	1
2	Do these objectives clearly address the research focus/problem?	1	1	1	1	1	1	1	1	1	1
3	Is the case control research method suitable to answer the research question?	1	1	1	1	1	1	1	1	1	1
4	Are the cases representative of the designated population?	1	1	1	1	1	1	1	1	1	1
5	Was the selected control group appropriate and acceptable?	1	1	1	1	1	1	1	1	1	1
6	Is this research instrument valid and reliable?	1	1	1	1	1	1	1	1	1	1
7	Is there a confounding of multiple pregnancies?	1	0	1	0	0	1	0	0	1	1
8	Are the results applicable to your research?	1	1	1	1	1	1	1	1	1	1
9	Is effect size practically relevant?	1	1	1	1	1	1	1	1	1	1
10	Is the estimated effect correct?	1	1	1	1	1	1	1	1	1	1
11	Is there a confidence level interval?	1	1	1	1	1	1	1	1	1	1
12	Are the results applicable to the designated population?	1	1	1	1	1	1	1	1	1	1
Total of Score		12	11	12	12	12	12	12	12	12	12

Note: 1: Yes; 0: No

Table 2. Description of the main studies included in the primary study of the meta-analysis

Author (Year)	Country	Study Design	Sample Size		Population	Intervensi	Comparison	Outcome	AOR (95% CI)
			Case	Control					
www.thejmch.com		Case Control	200	82	Pregnant mother	Experiencing UTI	Abortion and multiple pregnancy.	Premature Delivery	AOR= 2.80 (1.63 to 4.98)
Alijahan et al. (2014)	Iran	Case Control	37	45	Pregnant mother	Experiencing UTI	Preeclampsia, gestational hypertension, and oligohydroamnion	Premature Delivery	AOR= 1.80 (1.00 to 3.20)
Bojorquez et al. (2020)	Peru	Case Control	40	54	Pregnant women under 20 years old.	Experiencing UTI	Preeclampsia, multiple pregnancy and premature rupture of membranes.	Premature Delivery	AOR= 2.68 (1.30 to 5.30)
D'souza et al. (2015)	India	Case Control	16	7	Pregnant women aged 18-40 years.	Experiencing UTI	No UTI	Premature Delivery	AOR= 2.61 (1.02 to 7.23)
Fetene et al. (2022)	Ethiopia	Case Control	44	30	Pregnant mother	Experiencing UTI	Pregnancy hypertension, and premature rupture of membranes.	Premature Delivery	AOR= 3.02 (1.65 to 5.51)
Mahapula et al. (2016)	Tanzania	Case Control	19	33	Pregnant women aged 18-34 years.	Experiencing UTI	Polyhydroamnion, and and multiple pregnancy.	Premature Delivery	AOR= 2.70 (1.20 to 6.10)
Soundarajan et al. (2016)	India	Case Control	61	71	Pregnant mother	Experiencing UTI	Gestational diabetes, and preeclampsia.	Premature Delivery	AOR= 1.57 (1.08 to 2.29)
Sureshbabu et al. (2019)	India	Case Control	23	7	Pregnant mother	Experiencing UTI	Anemia, gestational diabetes, and hypothyroidism.	Premature Delivery	AOR= 3.67 (1.39 to 9.68)
Temu et al. (2016)	Tanzania	Case Control	49	55	Pregnant mother	Experiencing UTI	Placenta previa, gestational hypertension, and labor induction.	Premature Delivery	AOR= 1.86 (1.11 to 3.09)
Wakeyo et al. (2020)	Ethiopia	Case Control	11	13	Pregnant mother	Experiencing UTI	Hypertension of pregnancy, HIV and history of prematurity.	Premature Delivery	AOR= 3.60 (1.10 to 11)

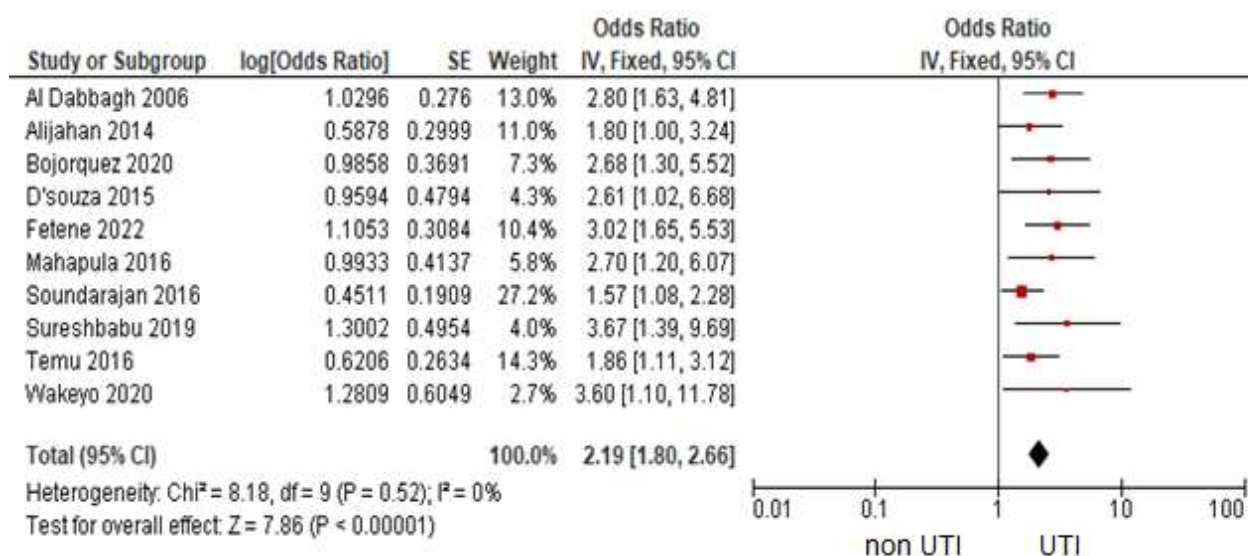


Figure 2. Funnel plot meta-analysis of the effect of urinary tract infections in pregnant women on preterm labor

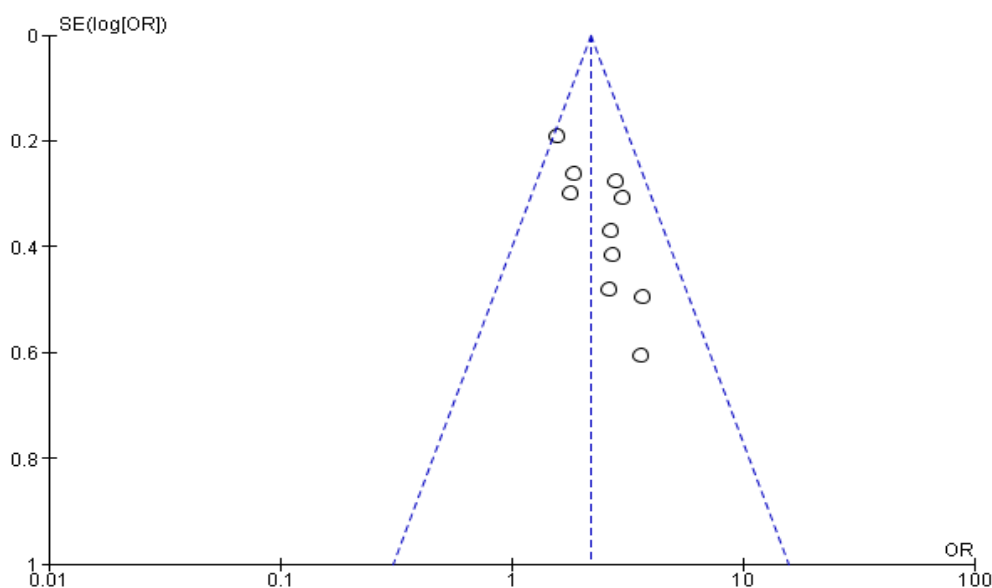


Figure 3. Funnel Plot meta-analysis of the effect of urinary tract infections in pregnant women on preterm labor

The Forest Plot in Figure 2 shows that the effect of urinary tract infection in pregnant women on preterm delivery was 2.19 times that of pregnant women without urinary tract infection (aOR= 2.19; 95% CI=1.80 to 2.66) and statistically significant $p < 0.001$. Statistical heterogeneity among studies is $I^2 = 0\%$, indicating a homogeneous data distribution (fixed effect model)

Funnel plots are plots that describe the approximate size of the effect of each study on its estimated accuracy, which is usually the standard error. The following funnel plot shows the risk of publication bias among the included studies.

Figure 3 shows that there is publication bias as evidenced by the distribution of plots that are not symmetrical, overesti-

mate, and that there is an imbalance in the distance between studies on the right and left sides of the funnel plot.

DISCUSSION

Premature labor is the onset of labor or delivery before 37 weeks of gestation. Labor is defined as cervical dilatation of more than 2 cm and there are regular and painful contractions or his (Datta et al., 2010). Risk factors associated with preterm delivery in conditions with a low neonatal mortality rate and a good index of maternal and child health services include pregnancy-induced hypertension (PIH), abnormal amniotic fluid volume, premature rupture of membranes, history of previous preterm delivery, history of infection urinary tract during pregnancy, systemic diseases such as bronchial asthma, heart defects, anemia, diabetes mellitus and chronic hypertension are independent risk factors for preterm labor (Goldenberg et al, 2008).

In this meta-analysis, the theme of the effect of urinary tract infections in pregnant women on preterm labor. The independent variable is urinary tract infection and the dependent variable is preterm delivery. Intervention is experiencing urinary tract infection. This study is important because urinary tract infections in pregnant women will affect the occurrence of preterm labor. Research that discusses preterm labor is considered important because preterm labor is a problem in increasing infant mortality, both in developing and developed countries. In this meta-analysis, the sample size was more than 500 pregnant women with urinary tract infections from ten case-control studies conducted in Iran, Iraq, India, Tanzania, Ethiopia, and Peru. This study uses studies from 2006 to 2022, each article has an aOR statistical outcome. In this study, it was explained that pregnant women with urinary tract infections had 2.19 times

more likely to experience preterm labor than pregnant women who did not experience urinary tract infections (aOR= 2.19; 95% CI=1.80 to 2.66) and statistically significant $p < 0.001$. This meta-analysis study provides evidence that there is an influence of pregnant women with urinary tract infections on preterm labor. In this study, there is a tendency for publication bias shown by funnel plots with an asymmetric distribution of plots.

The results of this study are similar to the research conducted by Kiran et al. (2010) who explained that there was a relationship between urinary tract infections in pregnant women and preterm labor. Pregnant women with urinary tract infections were more likely to give birth prematurely (20.34%; aOR= 5.05; 95% CI= 1.16 to 21.8). Faneite et al. (2006) also explained that pregnant women with urinary tract infections were at risk for preterm labor (aOR= 2.46; 95% CI= 1.19 to 5.07). Pregnant women who experience urinary tract infections occur when the membranes of the amniotic sac around the baby weaken. This can cause premature rupture of the membranes and premature labor (Sebayang et al., 2012).

Urinary Tract Infection (UTI) is a condition where germs or microbes grow and multiply in the urinary tract in significant numbers (IDAI, 2011). Infection can increase the release of inflammatory chemokines and cytokines such as interleukins and tumor necrosis factor. Microbial endotoxins and proinflammatory cytokines stimulate the production of prostaglandins (other inflammatory mediators) and matrix-degrading enzymes that ultimately result in stimulation of uterine contractions, premature rupture of membranes, and preterm delivery (Rodrigues et al, 2008). The organisms that cause urinary tract infections in pregnancy are uropathogens that

have proteins found on the cell surface that increase bacterial adhesion leading to increased virulence. Urinary catheterization is often done during labor can also lead to an increase in bacteria that cause urinary tract infections. In the postpartum period, changes in bladder sensitivity and bladder overdistention may predispose to urinary tract infections (Habak et al, 2021).

The limitations of this study are that it only uses three databases, and the language used only uses English articles.

AUTHOR CONTRIBUTION

Raras Indung Palupi as the main researcher who chose the topic, conducted a search for data collection in this study. Vitri Widyaningsih and Bhisma Murti conducted data analysis and reviewed research documents.

FUNDING AND SPONSORSHIP

This study is self-funded.

CONFLICT OF INTERESTS

There is no conflict of interest in this study.

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REFERENCES

- Abanto-Bojorquez D, Soto-Tarazona A (2020). Urinary tract infection and threatened preterm delivery in teenage pregnancies of a peruvian hospital. *Rev Fac Med Hum.* 20(3). <http://dx.doi.org/10.25176/rfmh.v20i3.3056>.
- Al-Dabbagh SA, Al-Taee WY (2006). Risk factors for pre-term birth in Iraq. *BMC Pregnancy Childbirth.* 6: 13. <https://doi.org/10.1186/1471-2393-6-13>.
- Alijahan R, Hazrati S, Mirzarahimi M, Pourfarzi F, Hadi P (2014). Prevalence and risk factors associated with preterm birth in Ardabil, Iran. *Iran J Reprod Med.* 12(1): 47–56. <https://pubmed.ncbi.nlm.nih.gov/24799861>.
- Cunningham F G, Leveno K J, Bloom S L, Hauth, J C, Rouse DJ, dan Spong C Y (2013). *Obstetri William.* 2: 369–370. Jakarta: EGC.
- Cochrane (2014). *RevMan 5.3 User Guide.* The Cochrane Collaboration.
- D'souza A, Gupta G, Mahindru D, Walia M , Katumalla F, Goyal S (2015). Genitourinary infections as a risk factor for preterm prelabour rupture of membranes: a hospital based case control study. *Int J Reprod, Contraception, Obstet, Gynecol.* 4(6). <http://dx.doi.org/10.18203/2320-1770.ijrcog2015-0785>.
- Fetene G, Tesfaye T, Negesse Y , Dulla D (2022). Factors associated with preterm birth among mothers who gave birth at public Hospitals in Sidama regional state, Southeast Ethiopia: Unmatched case-control study. *PLoS ONE* 17(4): e0265594. <https://doi.org/10.1371/journal.pone.0265594>.
- Habak P, Robert P. Griggs, Jr (2021). *Urinary tract infection in pregnancy.* Treasure Island (FL): StatPearls Publishing.
- Heidar NFA, Degheili JA, Yacoubian AA, Khauli RB (2019). Management of urinary tract infection in women: A practical approach for everyday practice. *Urol Ann.* 11(4): 339-346. https://doi.org/10.4103%2FUUA.UA_104_19.
- Kaur R, Rajinder Kaur (2020). Symptoms, risk factors, diagnosis and treatment of urinary tract infections. *Postgrad Med J.* (1154): 803-812. DOI: 10.113-

- 6/postgradmedj-2020-139090.
- Loh K, Sivalingam N (2007). Urinary tract infections in pregnancy. *Malays Fam Physician*. 2(2): 54-70. <http://www.ncbi.nlm.nih.gov/pmc/articles/pmc4170332/>.
- Mahapula F, Kumpuni K, Mlay J, Mrema T (2016). Risk factors associated with pre-term birth in Dar es Salaam, Tanzania. *Tanzania Journal of Health Research*, 18(1). <https://doi.org/10.4314/thrb.v18i1.4>.
- Masteryanto H, Gatut Hardianto, Herman-to Tri Joewono, Eko Budi Koendhori (2015). Infeksi saluran kemih sebagai faktor risiko terjadinya ancaman persalinan preterm. *Obstetri Ginekologi*. 23(2): 75-81. DOI: 10.20473/mog.v-23i2.2093.
- Mireles A, Jennifer N Walker, Michael Caparon and Scott J Hultgren (2015). Urinary tract infections: epidemiology, mechanisms of infection and treatment options. *Nat Rev Microbiol*. 13: 269–284. DOI: 10.1038/nrmicro3432.
- Murti B (2018). Prinsip dan metode riset epidemiologi (epidemiological research principles and methods). *Karanganar : Bintang Fajar Offset*.
- WHO (2018). Preterm Birth. Retrieved from: www.who.int. Accessed November 15, 2021.
- Rodrigues T, Rocha L, Barros H (2018). Physical abuse during pregnancy and preterm delivery. *AM J Obstet Gynecol*. 198:1-6.
- Sureshbabu R, Aramthottil P, Anil N, Sumathy S, Varughese S, Sreedevi A, Sukumaran S (2021). Risk factors associated with preterm delivery in singleton pregnancy in a tertiary care hospital in South India: A case control study. *Int J Womens Health*. 13: 369-377. <https://doi.org/10.2147/ijwh.s2-82251>.
- Soundarajan P, Muthuram P, Veerapandi M, Mariappan R (2016). Retrospective study factors related to preterm birth in Government Raja Mirasudar hospital and obstetric and perinatal outcome. *Int J Reprod, Contraception, Obstet, Gynecol*. 5(9). <http://dx.doi.org/10.18203/2320-1770.ijrcog-20162974>.
- Temu T, Masenga G, Obure J, Mosha D, Mahande M (2016). Maternal and obstetric risk factors associated with preterm delivery at a referral hospital in northern-eastern Tanzania. *Asian Pac J Reprod*. 5(5): 365-370. <https://doi.org/10.1016/j.apjr.2016.07.009>.
- SDKI (2017). Laporan pendahuluan survey demografi dan kesehatan Indonesia. in survey demografi dan kesehatan Indonesia 2017. Retrieved from: <https://doi.org/10.1111/j.14710528.2-007.01580.x>.
- Wakeyo D, Addisu Y, and Mareg M (2020). Determinants of Preterm Birth among mothers who gave birth in dilla university referral hospital, Southern Ethiopia. *Biomed Res Int*. 2020: 7031093. <https://doi.org/10.1155/2020/7031093>.
- Zulaikha N, Minata F (2021). Analisa determinan kejadian kelahiran prematur di RSIA Rika Amelia Palembang (Analysis of determinants of premature birth in RSIA Rika Amelia Palembang). *Jurnal Kesehatan Saemakers PER-DANA*. 4:1. <https://doi.org/10.32524/jksp.v4i1.3>.