

Outcome of Pregnancy with Intrauterine Device *In Situ*: A Meta-analysis

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ABSTRACT

Introduction: Intrauterine devices (IUDs) constitute the second-most used contraceptive method worldwide. Pregnancy in the presence of IUD results in obstetric complications. This study aims to review the outcome of intrauterine pregnancies among IUD removed, IUD retained, and no IUD.

Materials and methods: There were 89, 8, and 52 studies found in Pubmed®, Cochrane Library®, and Ovid® database. We included cohort or case-control studies consisting of minimally two groups: (i) no IUD and IUD retained or (ii) IUD removed and retained. Several outcomes were assessed, including preterm birth, miscarriage, premature rupture of membrane (PROM), placental abruption, placental previa, intrauterine growth restriction, chorioamnionitis, and cesarean delivery. The analysis of this meta-analysis used review manager 5.3.

Results: There were 7 studies included owing to language barrier and accessibility of article. Pregnancy with IUD *in situ* increased the risk of miscarriage (RR 6.50; 95% CI 4.56–9.28), PROM (RR 1.88; 95% CI 0.98–3.62), placenta previa (RR 2.33; 95% CI 1.14–4.73), placental abruption (RR 4.51; 95% CI 2.82–7.20), chorioamnionitis (RR 6.07; 95% CI 3.91–9.42), and cesarean delivery (RR 1.33; 95% CI 1.03–1.71). Meanwhile, IUD removed decreased the risk of miscarriage (RR 0.51; 95% CI 0.39–0.66) and preterm birth (RR 0.57, 95% CI 0.38–0.86) compared with IUD retained.

Conclusion: Conceiving with IUD in pregnancy increases the rate of miscarriage, placenta previa, abruption, chorioamnionitis, and cesarean delivery. Meanwhile, IUD removed early in pregnancy decreases the rate of miscarriage and preterm birth.

Keywords: Intrauterine device, Intrauterine pregnancy, Outcome.

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INTRODUCTION

Intrauterine devices (IUDs) constitute the second-most used contraceptive method worldwide; it is safe, effective, and widely used as the fifth most common among the modern contraception methods in USA.¹ In Indonesia, on the basis of Profil Kesehatan Indonesia 2016, IUD users became the fourth highest contraceptive-device users after injection, pill, and implant users, with a prevalence of 7.23% and 10.61% among new and active users, respectively.² The failure rate of this method ranges from 0.8% to 2.3%.^{3,4} The presence of IUD causes local inflammation through releasing prostaglandins and leukocytes from the endometrium (also progesterone from certain device) to create a hostile environment for oocytes and sperms. Besides, copper has a spermatocytic effect to prevent pregnancy.⁵

Pregnancy in the presence of IUD results in obstetric complications; therefore, removal of IUD during the first trimester of pregnancy is recommended to prevent septic complication and miscarriages.^{6,7} Hadas et al.⁸ stated that IUD retained in pregnancy increased several risks such as preterm delivery and chorioamnionitis. Meanwhile, on the basis of studies from 1970s to 1980s with a limited number of samples, the World Health Organization (WHO) recommends ruling out of ectopic pregnancy in the presence of IUD. Apart from that, removing IUD improves pregnancy outcomes if the IUD strings are visible or can be retrieved safely from the cervical canal.⁹ However, there are still limited studies discussing between IUD removed and retained in pregnancy to the outcome. Therefore, this study aims to review the outcome of intrauterine pregnancy among IUD removed, IUD retained, and no IUD.

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MATERIALS AND METHODS

Criteria for Considering Studies for this Review

Types of Studies

Cohort and case-control studies that investigate the intrauterine pregnancy outcome either IUD retained vs no IUD or IUD removed vs retained.

Type of Participants

Studies that described intrauterine pregnancy outcomes in women who had Copper T 380A-IUD *in situ* during conception.

Type of Comparison

The studies included in our review should consist of minimally two groups: no IUD and IUD retained, or IUD removed and retained.

Type of Outcome

We assessed several outcomes, including preterm birth, miscarriage, premature rupture of membrane (PROM), placental abruption, placental previa, intrauterine growth restriction, chorioamnionitis, and cesarean delivery.

Search Methods for Identification of Studies

We did not impose any language or other restrictions on the beginning of searches.

Electronic Searches

The search was conducted on Pubmed®, Cochrane Library®, and Ovid®. In PubMed, the search included keywords using the MeSH, namely "Pregnancy outcome AND Intrauterine Devices". Meanwhile, in Cochrane, the MeSH descriptor consisted of (Pregnancy) AND (Intrauterine device). The author used keywords of intrauterine pregnancy and (pregnancy complication or pregnancy outcome) and an intrauterine device in Ovid. In this searching strategy (performed on August 15th 2018), there were 89, 8, and 52 studies in Pubmed®, Cochrane Library®, and Ovid® database, respectively. The articles were screened using criteria such as abstracts answering the clinical questions, written in English language, full-text paper availability, and omitting all duplication papers. The analysis of this meta-analysis used review manager 5.3.

Data Collection and Analysis

Selection of Studies

Our search generated a list of abstracts. Two review authors (RS and ER) independently screened these abstracts. Studies that were not relevant were excluded at this stage. Any uncertainty on the eligibility of the studies that was based on title and abstract made the reviewers read full paper. The study flow diagram was shown in Flowchart 1.

Assessment of Risk of Bias in Included Studies

The risk of bias within the study was assessed using the Cochrane risk of bias table.

Assessment of Heterogeneity

Heterogeneity was assessed through the score of I^2 , which consisted of $I^2 < 50\%$ as homogeneity among studies.

RESULTS

The best study design to answer prognostic question is cohort studies. In this review, there were 10 articles related to the topic; however, only 7 studies included owing to language barrier and accessibility of article. The flow of literature through the assessment process for the update of this review is shown in Flowchart 1.

Included Studies

The studies included in meta-analysis are shown in Table 1.

Risk of Bias included Studies

Figure 1 described the risk of bias summary. Allocation concealment, blinding of participants and personnel, and blinding of outcome assessment could not be determined owing to prognostic study.

Pregnancy Outcomes

Of the studies included in the meta-analysis, there were several pregnancy outcomes between IUD and no IUD (Table 2) and IUD removed and retained (Table 3).

DISCUSSION

The limitation of this review was no proceedings of conferences were included and timing of IUD removal was not specified clearly. Of the studies included in this meta-analysis, there were three studies showing unclear or high risk of selection bias, such as Howard et al.,¹⁰ Skjeldestad et al.,⁷ and Chaim et al.¹¹ The first study by Howard et al.¹⁰ did not mention clearly whether subjects were asked for the time of IUD removal. Meanwhile, Skjeldestad et al.⁷ started the study from all pregnant women to search the presence of IUD and Chaim et al.¹¹ designed a case-control study by comparing 1 and 3 for case and control subjects. However, this was the first meta-analysis which summarized all studies focusing on IUD removed, retained, and no IUD to the pregnancy outcome.

Flowchart 1: Study flow diagram in this review

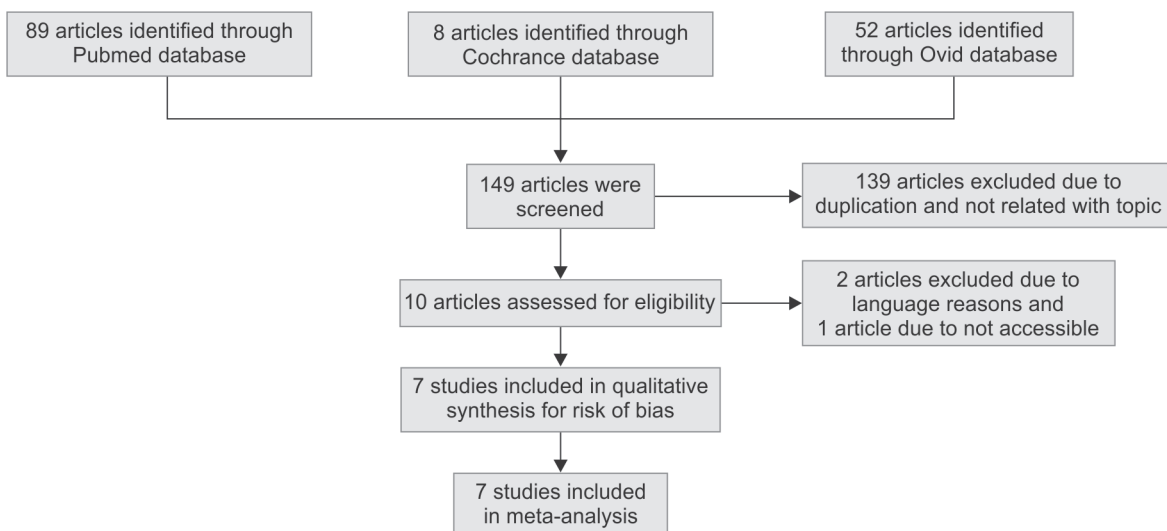


Table 1: Characteristics of study included in meta-analysis

Study	Methods	Participants	Outcomes
Howard et al. ¹⁰	Prospective study	275 pregnant women who conceived with a copper T <i>in situ</i>	IUD retained group: 85 (54.1%) spontaneous abortion, 12 (17.4%) preterm birth IUD removed group: 24 (20.3%) spontaneous abortion, 4 (4.3%) preterm birth
Skjeldestad et al. ⁷	Retrospective study	1,032 women who became pregnant was investigated for the presence of IUD	IUD <i>in situ</i> : 12 (15.6%) spontaneous abortion No IUD: 116 (7%) spontaneous abortion
Chaim et al. ¹¹	Case control study	16 multiparous women who conceived with a copper IUD <i>in situ</i> and 48 women matched as control group without IUD	IUD <i>in situ</i> : 3 (18.7%) preterm No IUD: 1 (2%) preterm
Hadas et al. ⁸	Retrospective study	292 pregnant women with an IUD and all IUDs were copper-based devices	IUD retained group: 1% IUGR, 8.2% malpresentation, 10.2% PROM, 4.1% placental abruption, 4.1% placenta previa, 18.4% preterm delivery, 31.6% cesarean delivery, 7.1% chorioamnionitis IUD removed group: 0.5% IUGR, 8.8% malpresentation, 7.7% PROM, 2.1% placental abruption, 0.5% placenta previa, 14.4% preterm delivery, 20.6% cesarean delivery, 4.1% chorioamnionitis
Sun et al. ¹²	Retrospective cohort study	12,297 pregnancies of which 196 had a copper T 380A IUD <i>in situ</i> during pregnancy	No IUD: 1.7% IUGR, 4.9% malpresentation, 5.7% PROM, 0.7% placental abruption, 0.5% placenta previa, 7.3% preterm delivery, 12.8% cesarean delivery, 0.7% chorioamnionitis IUD <i>in situ</i> : 110 (56.1%) preterm birth, 31 (15.8%) miscarriage, 10 (5.1%) SGA, 16 (8.2%) clinical chorioamnionitis, 16 (8.2%) placental abruption, 4 (2%) placenta previa, 61 (31.1%) cesarean delivery
Ruya et al. ¹³	Prospective study	48 women who conceived an intrauterine pregnancy with IUD and decided to continue pregnancy of at least 12 weeks of gestation and all IUDs were copper T 380A	No IUD: 2,503 (20.7%) preterm birth, 146 (1.2%) miscarriage, 1,141 (9.4%) SGA, 209 (1.7%) clinical chorioamnionitis, 249 (2.1%) placental abruption, 186 (1.5%) placenta previa, 3,765 (31.1%) cesarean delivery
Seval et al. ¹⁴	Retrospective cohort study	30 pregnant women with IUD-retained and 114 with IUD-removed	IUD retained group: 12 (45%) PROM, 16 (53.3%) miscarriage, 7 (30%) preterm birth, 2 (6.7%) placental abruption, 2 (6.7%) SGA IUD removed group: 0 PROM, 3 (16.7%) miscarriage, 1 (5.6%) preterm birth, 0 placenta abruption, 2 (11.1%) SGA IUD retained group: 5 (16.7%) preterm birth, 15 (50%) miscarriage, 0 intrauterine growth retardation, 2 (12.5%) PPROM, 8 (50%) cesarean section IUD removed group: 13 (11.4%) preterm birth, 28 (4.6%) miscarriage, 2 (2.3%) intrauterine growth retardation, 2 (2.3%) PPROM, 38 (44.2%) cesarean section



	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding of participants and personnel (performance bias)	Blinding of outcome assessment (detection bias)	Incomplete outcome data (attrition bias)	Selective reporting (reporting bias)	Other bias
Chaim 1992	⊖				⊕	⊕	
Deever 2011	⊕				⊕	⊕	
Ganer 2009	⊕				⊕	⊕	
Kim 2010	⊕				⊕	⊕	
Ozguerding 2004	⊕				⊕	⊕	
Skjeldestad 1988	⊖				⊖	⊖	
Tatum 1976	?				⊕	?	

Fig. 1: Risk of bias summary for each study

Table 2: Outcomes of pregnancy in group of IUD and no IUD

IUD vs No IUD	RR	95% CI	p	I ²
Miscarriage	6.50	4.56–9.28	<0.001	96%
Preterm birth	1.06	0.91–1.24	0.47	91%
PROM	1.88	0.98–3.62	0.06	N/A
Placenta previa	2.33	1.14–4.73	0.02	87%
Placental abruption	4.51	2.82–7.20	<0.001	0%
Chorioamnionitis	6.07	3.91–9.42	<0.01	63%
Intrauterine growth restriction	0.95	0.59–1.50	0.81	97%
Cesarean delivery	1.33	1.03–1.71	0.03	93%

RR, relative risk; CI, confidence interval
 PROM, premature rupture of membrane; N/A, not available

Of all studies that included IUD retained and removed, only studies by Seval et al.¹⁴ and Ruya et al.¹³ used ultrasound examination to reveal visible copper IUD in the uterine cavity. After this examination, Ruya et al.¹³ and Hadas et al.⁸ showed explicitly that IUD removal was performed in the early gestation, namely first 12 weeks of gestation (trimester 1). Meanwhile, other studies did not mention clearly the time of IUD removal.

Compared with pregnancy without IUD, women who conceived with IUD had a higher rate of placental abruption. A previous

Table 3: Outcomes of pregnancy in group of IUD removed and retained

IUD removed vs retained	RR	95% CI	p	I ²
Miscarriage	0.51	0.39–0.66	<0.001	85%
Preterm birth	0.57	0.38–0.86	0.007	33%
PROM	0.51	0.25–1.05	0.07	62%
Placenta previa	0.13	0.01–1.11	0.06	N/A
Placental abruption	0.51	0.13–1.98	0.33	N/A
Chorioamnionitis	0.58	0.22–1.55	0.27	N/A
Intrauterine growth restriction	0.82	0.11–5.93	0.84	0%
Cesarean delivery	0.79	0.57–1.08	0.14	29%

RR, relative risk; CI, confidence interval
 PROM, premature rupture of membrane; N/A, not available

study stated that chronic inflammatory process of placenta lead to placental abruption. Apart from that, chronic inflammatory process activated cytokines, such as interleukin-1β and tumor necrosis factor-α.¹⁵ This was also associated with chorioamnionitis. Neutrophil infiltration to fetal membrane ended to preterm PROM and placental abruption, suggesting that enhanced protease activity and inflammatory cytokines had a role in placental abruption.¹⁶ Sun et al.¹² suggested that inflammatory state due to IUD in situ during pregnancy contributed to the risk of placental abruption, preterm PROM, spontaneous preterm labor with intact membrane. In this meta-analysis, the author found all complications related to IUD in pregnancy caused a higher rate of cesarean delivery.

This meta-analysis revealed that conceiving with IUD leads to significant risk factors for maternal outcomes. The IUD removed early in pregnancy decreased the rate of miscarriage and preterm birth; however, an IUD in pregnancy increased the risk of miscarriage, placenta previa, placental abruption, chorioamnionitis, and cesarean delivery compared with normal pregnancy without IUD. It was corresponding to previous systematic review in 2012, which showed that women with a retained IUD had a greater risk for spontaneous abortion, preterm delivery, and septic abortion. Meanwhile, compared with women who conceived without IUD, this systematic review showed a higher risk for spontaneous abortion, preterm delivery, and chorioamnionitis even after the IUD removal in early pregnancy.¹⁷ Chorioamnionitis in IUD retained is reactive inflammation owing to the presence of a foreign body; so it evolve to secondary infection;⁸ however, IUD removal in this meta-analysis was not differently significant to IUD retained in pregnancy.

CONCLUSION

Conceiving with IUD in pregnancy increases the rate of miscarriage, placenta previa, abruption, chorioamnionitis, and cesarean delivery. Meanwhile, IUD removed early in pregnancy decreases the rate of miscarriage and preterm birth.

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