

## Research Article

# Spontaneous Pregnancy Rates with and without Ovulation Induction after Post-Laparoscopic Neosalpingostomy for Stage III–IV Hydrosalpinx

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## Abstract

**Objective:** To compare pregnancy outcomes between natural conception and ovulation induction following laparoscopic neosalpingostomy in women with stage III–IV hydrosalpinx.

**Methods:** A quasi-experimental study was conducted between 2014 and 2019 involving 70 infertile women who underwent laparoscopic neosalpingostomy. Participants were assigned to either a natural conception group or an ovulation induction group receiving clomiphene citrate and estradiol valerate. Patients were followed for six to seven months postoperatively. Pregnancy outcomes were analyzed using the chi-square test and multivariate logistic regression, with statistical significance set at  $p < 0.05$ .

**Results:** The overall pregnancy rate was 83% within seven months after surgery. Forty-one pregnancies occurred in the natural conception group. No significant association was found between ovulation induction or maternal age  $>35$  years and term pregnancy ( $p > 0.05$ ). Ectopic pregnancy occurred in 4–5% of cases. Multivariate logistic regression analysis identified no independent predictors of term pregnancy.

**Conclusion:** Laparoscopic neosalpingostomy remains a viable fertility-preserving treatment option for women with advanced hydrosalpinx. Pregnancy outcomes were comparable between women who conceived naturally and those who received ovulation induction therapy.

**Keywords:** hydrosalpinx, laparoscopic neosalpingostomy, pregnancy outcomes, spontaneous pregnancy.

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## INTRODUCTION

Infertility remains a significant health issue worldwide, including in Indonesia. Although it does not impair physical functioning and is not life-threatening, infertility can substantially affect the quality of life of couples by causing medical, economic, and psychological burdens. Infertility is defined as the inability to achieve pregnancy after 12 months of regular, unprotected sexual intercourse in the absence of known reproductive pathology.<sup>1,2</sup>

Infertility may result from female factors, male factors, or a combination of both. However, a substantial proportion of infertility cases are attributed to female factors. Various risk factors contribute to female infertility, including advanced maternal age, occupation, stress, Body Mass Index (BMI), and abnormalities of the reproductive organs. These abnormalities may involve ovulatory dysfunction, tubal and pelvic disorders, and uterine abnormalities.<sup>3–5</sup>

Disorders of the female reproductive organs, particularly tubal pathology, are important

contributors to infertility. Studies have shown that women with reproductive tract abnormalities are at a higher risk of infertility than those without such conditions. Fallopian tube obstruction, frequently accompanied by hydrosalpinx, may impair fertility through embryotoxic effects and disruption of normal ciliary function and embryo transport within the fallopian tubes.<sup>6–12</sup>

For women with distal tubal obstruction and hydrosalpinx, corrective surgical procedures such as peritubal adhesiolysis, fimbrioplasty, and neosalpingostomy are recommended and are commonly performed laparoscopically. These procedures may be considered for patients who wish to preserve their fertility and achieve spontaneous pregnancy. Laparoscopic neosalpingostomy represents a fertility-preserving alternative for women who prefer to avoid salpingectomy and assisted reproductive technologies such as Intrauterine Insemination (IUI) or in Vitro Fertilization (IVF).<sup>13–15</sup>

The present study aimed to compare pregnancy outcomes between women who conceived naturally and those who underwent ovulation induction following laparoscopic neosalpingostomy for stage III–IV hydrosalpinx.

## METHODS

This quasi-experimental study was conducted at Anugerah Women & Children Hospital, Semarang, Indonesia, between January 2014 and December 2019. Ethical approval was obtained from the Health Research Ethics Committee of the Faculty of Medicine, Universitas Diponegoro (No. 380/EC/KEPK.FK-UNDIP/X/2021). Written informed consent was obtained from all participants, including consent for surgery, postoperative monitoring, teleconsultation follow-up, and the use of clinical data for research purposes.

Women with primary infertility who underwent laparoscopic neosalpingostomy for bilateral stage III–IV hydrosalpinx were eligible for inclusion. Diagnosis was confirmed by hysterosalpingography (HSG). Additional inclusion criteria included normal semen parameters according to WHO criteria and willingness to participate in teleconsultation follow-up. Patients who preferred immediate Assisted Reproductive Technology (ART), had abnormal sperm factors, or declined follow-up were excluded.

Participants were allocated into two groups: a natural conception group and an ovulation induction group. Patients in the ovulation induction group received clomiphene citrate 100 mg daily (two 50-mg tablets) from cycle days 2–6 and estradiol valerate 2 mg daily from cycle days 8–12. Treatment was administered for three consecutive cycles, followed by three months of observation without medication.

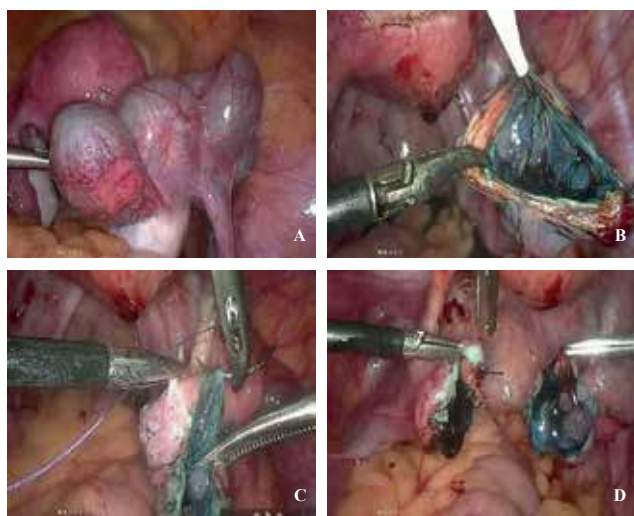
All patients underwent baseline Transvaginal Ultrasonography (TVS) on cycle day 2 before treatment initiation. Serial TVS examinations were performed from cycle day 8 and repeated every 1–3 days to monitor follicular development and endometrial thickness until at least one follicle reached a mean diameter of  $\geq 18$  mm. Patients were followed for six months after intervention. This follow-up period was selected because most spontaneous or treatment-assisted conceptions after tubal reconstructive surgery occur within the first 6–12 months postoperatively.

The laparoscopic procedure was performed using the Erbe VIRON 1 Laparoscopy System®. Hydrosalpinx severity was classified according to the Donnez and Casanas-Roux classification based on preoperative HSG findings. Grade I was defined as a phymotic ostium with preserved tubal patency, grade II as complete distal tubal occlusion without ampullary dilatation, grade III as ampullary dilatation  $< 2.5$  cm with preserved ampullary folds, grade IV as hydrosalpinx with ampullary dilatation  $> 2.5$  cm and preserved ampullary folds, and grade V as thick-walled hydrosalpinx with loss of ampullary folds. Only patients with grade III and IV hydrosalpinx were included in this study. Pelvic adhesions were graded according to the American Fertility Society classification.<sup>16</sup> Representative laparoscopic findings of bilateral fimbrial phimosis with stage III–IV hydrosalpinx are shown in Figure 1.



**Figure 1.** Laparoscopic appearance of bilateral distal tubal occlusion (fimbrial phimosis) associated with stage III–IV hydrosalpinx before neosalpingostomy

Distal tubal obstruction caused by fimbrial phimosis, with or without hydrosalpinx, was treated by adhesiolysis followed by salpingostomy. The distal fimbrial end was opened using a monopolar needle (40 W, pure-cut mode) under laparoscopic guidance until the fimbriae became visible.<sup>10,17,18</sup> To prevent re-occlusion, fimbrioplasty (Bruhat procedure) was performed using 6-0 monofilament sutures placed at four corners of the opened fimbria. Together, salpingostomy and fimbrioplasty constituted the neosalpingostomy procedure.<sup>19,20</sup> The main surgical steps are illustrated in Figure 2.



**Figure 2.** Surgical steps of laparoscopic neosalpingostomy. (A) Fimbrial phimosis with hydrosalpinx. (B) Creation of salpingostomy. (C) Fimbrioplasty with suturing of the fimbrial edges. (D) Final reconstructed fimbrial ostium after neosalpingostomy.

Pregnancy outcomes, including term pregnancy and ectopic pregnancy, were recorded during follow-up. Data were analyzed using STATA software. Continuous variables were expressed as mean  $\pm$  standard deviation, whereas categorical variables were presented as frequencies and percentages. Associations between clinical variables and pregnancy outcomes were assessed using the Chi-square test or Fisher's exact test, as appropriate. Relative risks (RRs) with 95% confidence intervals (CIs) were calculated. Multivariate logistic regression analysis was performed to identify independent predictors of term pregnancy, including maternal age ( $>35$  vs.  $\leq 35$  years), duration of infertility ( $>5$  vs.  $\leq 5$  years), hydrosalpinx grade (III vs. IV), and ovulation induction status. Adjusted odds ratios (AORs) with 95% CIs were reported. Variables with  $p < 0.25$  in bivariate analysis were included

in the multivariate model. Statistical significance was defined as  $p < 0.05$ .

## RESULTS

A total of 72 women met the eligibility criteria and were enrolled in the study. Two patients were lost to follow-up, resulting in 70 women included in the final outcome analysis.

Baseline characteristics of the enrolled participants are presented in Table 1. Most women were older than 35 years (77.8%), with a mean age of 38.7 years. The majority had experienced infertility for more than five years (81.9%), with a mean infertility duration of 8.2 years.

**Table 1.** Baseline Characteristics of Enrolled Participants (N = 72)

| Variable                               | n (%)     | Mean |
|----------------------------------------|-----------|------|
| <b>Maternal age (years)</b>            |           |      |
| $\leq 35$                              | 16 (22.2) | 32.5 |
| $> 35$                                 | 56 (77.8) | 38.7 |
| <b>Duration of infertility (years)</b> |           |      |
| $\leq 5$                               | 13 (18.1) | 3.7  |
| $> 5$                                  | 59 (81.9) | 8.2  |

Among the 70 women included in the final analysis, 41 underwent ovulation induction using clomiphene citrate and estradiol valerate (CC+EE), whereas 29 attempted natural conception. Overall, 58 women (82.9%) achieved pregnancy within seven months after laparoscopic neosalpingostomy, while 12 women (17.1%) did not conceive.

Clinical outcomes and hydrosalpinx characteristics are summarized in Table 2. Term pregnancy was achieved in 38 women (54.3%), while 16 women (22.9%) experienced miscarriage and four women (5.7%) developed ectopic pregnancy. Among women who delivered, 29 (76.3%) underwent cesarean section because of obstetric indications. Stage III hydrosalpinx was more common than stage IV hydrosalpinx (70.0% vs. 30.0%).

**Table 2.** Clinical Outcomes and Hydrosalpinx Characteristics (N = 70)

| Variable                       | n (%)     |
|--------------------------------|-----------|
| <b>Pregnancy outcome</b>       |           |
| Miscarriage                    | 16 (22.9) |
| Ectopic pregnancy              | 4 (5.7)   |
| Term pregnancy                 | 38 (54.3) |
| No pregnancy                   | 12 (17.1) |
| <b>Mode of delivery (n=38)</b> |           |
| Vaginal delivery               | 9 (23.7)  |
| Cesarean section               | 29 (76.3) |
| <b>Hydrosalpinx grade</b>      |           |
| Grade III                      | 49 (70.0) |
| Grade IV                       | 21 (30.0) |

Pregnancy outcomes according to treatment group are presented in Table 3. Term pregnancy occurred in 23 women (56.1%) in the ovulation induction group and 15 women (51.7%) in the natural conception group. Ectopic pregnancy occurred in one woman (2.4%) in the ovulation induction group and three women (10.3%) in the natural conception group. Miscarriage occurred in eight women in each group.

**Table 3.** Pregnancy Outcomes According to Treatment Group (N = 70)

| Outcome           | Ovulation Induction<br>(CC+EE) n=41 | Natural Cycle<br>n=29 |
|-------------------|-------------------------------------|-----------------------|
| Miscarriage       | 8 (19.5)                            | 8 (27.6)              |
| Ectopic pregnancy | 1 (2.4)                             | 3 (10.3)              |
| Term pregnancy    | 23 (56.1)                           | 15 (51.7)             |
| No pregnancy      | 9 (22.0)                            | 3 (10.3)              |
| Total             | 41 (100)                            | 29 (100)              |

Abbreviations: CC = Clomiphene Citrate; EE = Estradiol Valerate.

No statistically significant association was observed between maternal age >35 years and pregnancy outcomes ( $p > 0.05$ ). Although older women demonstrated a higher relative risk of ectopic pregnancy (RR 2.33; 95% CI 0.42–12.91), the association was not statistically significant because of the wide confidence interval.

Similarly, ovulation induction was not significantly associated with improved term pregnancy rates compared with natural conception ( $p > 0.05$ ). Although the proportion of term pregnancies was slightly higher in the ovulation induction group, the difference did not reach statistical significance.

Multivariate logistic regression analysis demonstrated that none of the evaluated variables, including maternal age (>35 vs. ≤35 years), duration of infertility (>5 vs. ≤5 years), hydrosalpinx grade (III vs. IV), and ovulation

induction status, were independent predictors of term pregnancy (all  $p > 0.05$ ). Maternal age >35 years showed a trend toward a lower likelihood of term pregnancy (AOR 0.74; 95% CI 0.41–1.68), whereas ovulation induction showed a non-significant trend toward a higher likelihood of term pregnancy (AOR 1.32; 95% CI 0.52–3.01).

## DISCUSSION

Tubal factor infertility caused by distal tubal occlusion and hydrosalpinx is responsible for approximately 20–30% of female infertility cases. Hydrosalpinx may impair fertility through embryotoxic effects and disruption of normal tubal ciliary function, thereby reducing the likelihood of successful fertilization and embryo transport.<sup>6–12</sup> In women who wish to conceive naturally and avoid immediate Assisted Reproductive Technology (ART), reconstructive tubal surgery remains a potential treatment option.<sup>10,11,14,15</sup>

In the present study, laparoscopic neosalpingostomy resulted in an overall pregnancy rate of 82.9% within seven months after surgery. Although no statistically significant difference was observed between women who conceived naturally and those who underwent ovulation induction, both groups achieved favorable reproductive outcomes. These findings support previous studies reporting pregnancy rates of approximately 60–70% following fimbrioplasty and neosalpingostomy in selected patients with hydrosalpinx.<sup>10,11,15</sup>

Ectopic pregnancy remains a recognized complication following tubal reconstructive surgery.<sup>21–25</sup> In this study, ectopic pregnancy occurred in 5.7% of patients despite postoperative HSG confirmation of tubal patency. This finding is consistent with previous reports and may be explained by residual tubal dysfunction, impaired ciliary activity, or persistent peri-adnexal adhesions that affect ovum transport.<sup>21–25</sup>

The severity of pelvic adhesions is an important determinant of reproductive outcomes after tubal surgery. Distal tubal occlusion associated with chronic pelvic inflammation frequently results in peri-adnexal adhesions involving the fimbriae and surrounding structures. Previous studies have shown that laparoscopic adhesiolysis is more effective than laparotomy in restoring pelvic anatomy and preserving reproductive function, particularly in patients with moderate-to-severe adhesions.<sup>16,18–20</sup>

Maternal age greater than 35 years was not significantly associated with pregnancy outcomes. Although older women showed a higher relative risk of ectopic pregnancy (RR 2.33; 95% CI 0.42–12.91), the wide confidence interval suggests limited statistical precision, likely related to the relatively small sample size. Likewise, ovulation induction was not significantly associated with an increased likelihood of term pregnancy.

From a biological perspective, ovulation induction using clomiphene citrate and estradiol valerate may provide additional reproductive benefits after tubal reconstructive surgery. Clomiphene citrate stimulates follicular development through modulation of estrogen receptors and increased endogenous gonadotropin secretion, thereby enhancing ovulation frequency. Estradiol supplementation may support endometrial receptivity, tubal epithelial regeneration, ciliary activity, and tubal motility during postoperative healing. Although these physiological mechanisms are plausible, the present study did not demonstrate a statistically significant advantage of ovulation induction over natural conception.

The findings of this study suggest that laparoscopic neosalpingostomy remains a viable fertility-preserving option for women with stage III–IV hydrosalpinx, particularly in settings where ART is unavailable, inaccessible, or financially burdensome. Recent studies have also demonstrated favorable reproductive outcomes following neosalpingostomy in selected patients with hydrosalpinx, supporting its role as a fertility-preserving procedure before IVF.<sup>26–30</sup> Patients should nevertheless be counseled regarding the risk of ectopic pregnancy and the possibility of requiring ART if conception does not occur within 6–12 months following surgery.

This study has several limitations. First, the relatively small sample size ( $n = 70$ ) may have limited the statistical power to detect significant differences between groups. Second, the follow-up period was limited to 6–7 months; therefore, long-term reproductive outcomes and cumulative live birth rates could not be evaluated. Larger multicenter studies with longer follow-up periods are warranted to further clarify the role of ovulation induction after laparoscopic neosalpingostomy.

## CONCLUSIONS

Laparoscopic neosalpingostomy may be considered a fertility-preserving surgical option for women with stage III–IV hydrosalpinx who desire natural conception and prefer to defer assisted reproductive technology (ART). In selected patients with preserved tubal morphology and favorable adhesion characteristics, neosalpingostomy may provide a cost-effective alternative before in vitro fertilization (IVF). Although ovulation induction did not significantly improve pregnancy outcomes compared with natural conception, both approaches achieved favorable pregnancy rates following surgery. Therefore, laparoscopic neosalpingostomy remains a reasonable treatment option for women with advanced hydrosalpinx before proceeding to ART.

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## CONFLICTS of INTEREST

There is no conflict of interest in this study

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