

A Comparison of the Incidence of Spontaneous Pregnancy Between Ovulation Induction and No Ovulation Induction in Patients After Post-Laparoscopic Neosalpingostomy with 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 from 2014–2019 including 70 infertile women undergoing laparoscopic neosalpingostomy. Participants were divided into natural cycle and ovulation induction groups (clomiphene citrate plus estradiol valerate). Follow-up lasted six to seven months. Pregnancy outcomes were analyzed using chi-square and multivariate logistic regression, with $p < 0.05$ considered significant.

Results:

The overall pregnancy rate was 83% within seven months postoperatively. Forty-one pregnancies occurred without induction. 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 analysis showed no independent predictors of term pregnancy.

Conclusion:

Laparoscopic neosalpingostomy remains a viable fertility-preserving option for women with advanced hydrosalpinx, with comparable outcomes between natural conception and ovulation induction.

Key words : Spontaneous pregnancy, hydrosalpinx, Laparoscopic Neosalpingostomy, Pregnancy outcomes

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INTRODUCTION

Infertility remains a health issue worldwide, including in Indonesia. Although it does not affect physical activity and is not life-threatening, it significantly impacts family life for many couples due to medical, economic, and psychological problems. Infertility is defined as the failure to conceive after 12 months of regular, unprotected sexual activity in the absence of reproductive pathology^{1, 2} Infertility can be caused by women, men, or both. However,

among the many infertile couples, most cases are due to female factors. A woman may be infertile because of various risk factors. These factors include age, occupation, stress level, body mass index related to nutritional status, and reproductive organ abnormalities, such as disorders of ovulation, tubal and pelvic issues, and uterine problems disorders.³⁻⁵

Factors related to abnormalities of female reproductive organs also contribute to infertility. According to the study's findings, women with reproductive organ disorders have a higher risk of infertility compared to those without such disorders. The issue of blocked fallopian tubes, often accompanied by swelling or hydrosalpinx, can lead to embryo damage through embryotoxic effects and mechanical disruption of ciliary hair movement within the fallopian tubes.⁶⁻¹² It is advised to perform corrections such as peritubal adhesiolysis, fimbrioplasty, and neosalpingostomy in cases of fallopian tube obstruction with hydrosalpinx, typically done laparoscopically. It is also recommended for patients who want to conceive naturally. Neosalpingostomy is a strategic alternative for those who are not willing to undergo salpingectomy but still desire a natural pregnancy without assisted technologies like IUI or IVF.¹³⁻¹⁵

The purpose of this study was to compare the pregnancy rates between patients who conceived naturally and those who successfully induced ovulation following laparoscopic neosalpingostomy for hydrosalpinx.

METHODS

This study employed a quasi-experimental design. It was conducted at Anugerah Women & Children Hospital in Semarang, Indonesia, from January 2014 to December 2019, and was approved by the Health Research Ethics Committee under the Ethical Clearance for Research No. 380/EC/KEPK.FK-UNDIP/X/2021. All patients provided written informed consent prior to participation in the study. Patients were informed about the surgical procedure, postoperative monitoring, potential risks including ectopic pregnancy, and the option of ovulation induction therapy. Consent for teleconsultation follow-up and data use for research purposes was also obtained. Data were analyzed using STATA statistical software. Descriptive statistics were used to summarize demographic and clinical characteristics. Continuous variables were presented as mean $\pm$ standard deviation, while categorical variables were expressed as frequencies and percentages. Bivariate analysis was performed using the Chi-square test or Fisher's exact test (when appropriate) to assess associations between categorical variables such as age group, ovulation induction status, and pregnancy outcomes. Relative risks (RR) with 95% confidence intervals (CI) were calculated to estimate the strength of association. A p-value less than 0.05 was considered statistically significant. The 6-month follow-up period was selected based on clinical evidence suggesting that most spontaneous or induced conceptions following tubal reconstructive surgery occur within the first 6–12 months postoperatively. Monitoring during this early period allows for the assessment of tubal patency before the risk of re-adhesion or tubal re-occlusion increases. Patients are divided into two groups based on hydrosalpinx. The first group comprises patients who decline ovulation induction, while the second group includes patients undergoing ovulation induction therapy with 10 mg of clomiphene citrate (Pinfetil 50 mg, Novell pharmaceutical laboratories), taking two tablets daily for five days from the 2nd to the 6th day of their cycle. Additionally, they receive 1 tablet of 2 mg estradiol valerate (Progynova, BAYER) daily for 5 days, from the 8th to the 12th day of the cycle.

Patients will be monitored over three cycles using the same therapy. Monitoring includes egg assessment via transvaginal ultrasound on day 12 to evaluate follicle size and endometrial

thickness, followed by a three-month period without therapy. The total monitoring period spans six months from the beginning of the intervention. All patients undergo basal transvaginal ultrasonography (TVS) The General Electric Voluson S10 Expert® on day 2 of their menstrual cycle before starting treatment. Serial TVS begins on cycle day 8 to assess follicular growth (number and diameter of follicles) and endometrial thickness. This assessment continues every 1–3 days until the mean follicular diameter (average of two orthogonal measurements) reaches ≥ 18 mm. The inclusion criteria for this study are patients who have undergone laparoscopic neosalpingostomy surgery due to bilateral fallopian tube phimosis with damage classified as grade III or grade IV. They are monitored in two groups and are willing to participate in teleconsultation. In addition to the wives' factors, the husbands' factors—specifically, normal sperm according to WHO criteria—are also required. Exclusion criteria include patients who are unwilling to be monitored by the teleconsultation system. They prefer to directly undergo pregnancy therapy with assisted technology due to abnormal sperm factors. If more than six months pass after the intervention in both groups and group 2 still has not achieved pregnancy, these patients will be excluded and advised to try pregnancy with assisted technology. Multivariate logistic regression analysis was conducted to identify independent predictors of term pregnancy following laparoscopic neosalpingostomy. Variables in the regression model included maternal age (>35 vs. ≤ 35 years), duration of infertility (>5 vs. ≤ 5 years), degree of hydrosalpinx (grade III vs. IV), and ovulation induction status. Adjusted odds ratios (AOR) with 95% confidence intervals were calculated. Variables with $p < 0.25$ in bivariate analysis were included in the multivariate model.

The study population comprises all women who self-referred for infertility evaluation at Anugerah Women & Children Hospital in Semarang, Indonesia. The control group consisted of women with problematic infertility examined at the same hospital's infertility clinic. The case subjects are women experiencing primary infertility with both non-patent tubal hydrosalpinx stages III and IV, confirmed by supporting examination, specifically HSG. The control group subjects are infertile women who underwent laparoscopic neosalpingotomy by Erbe VIRON 1 Laparoscopy System® without ovulation induction, operating on a natural cycle. They are compared with patients who receive ovulation induction with 10 mg of clomiphene citrate given on the 2nd day of menstruation and 2 mg of estradiol valerate on the 8th day of the cycle, according to inclusion criteria. The success of the procedure to open the fimbria in hydrosalpinx, as classified by Donnez and Casanas-Roux, based on preoperative HSG examination [table 1], is influenced by the degree of adhesion, according to the American Fertility Society classification adhesion.¹⁶

Table 1 presents the classification of the degree of fimbrial closure in the fallopian tube according to Donnez and Casanaz-Roux. In grade 1, the fimbrial ends are closed, but both tubes are open on a hysterosalpingography (HSG). At grade 2, both fimbriae are completely closed, and the HSG results show that both tubes are non-patent. Grades 3 and 4 are characterized by widening of the fallopian tubes. Meanwhile, in grade 5, there is thickening of the fallopian tube wall, leading to the loss of the folds in the entire ampulla of the fallopian tube.

In table 1, we can see the report during laparoscopic neosalpingostomy based on the American Fertility Society Classification of Adhesion, where the level of adhesion is higher. The closure of the distal part of the fimbria or phimosis of the fimbria, with or without hydrosalpinx, results from a chronic pelvic infection that causes adhesions. During laparoscopy, adhesiolysis is performed to free all parts of the fallopian tube from adhesions,

followed by gently holding the distal part of the tube with phimosi. A tube is then opened with phimosi. This is done using a 40-watt Erbe VIO 3[®] monopolar needle set to “pure cut” mode, without coagulation, until the phimosi is opened. Cross-slices are made with a monopolar needle under laparoscopic guidance until the distal part of the tube is opened and the fimbriae are visible. This procedure is called a salpingostomy.^{10,17,18} To prevent re-closure of the phimosi, suturing is continued with 6-0 monofilament threads at four corners of the opened fimbria, a technique known as the Bruhat procedure or fimbrioplasty. This is why adhesion is divided into mild, moderate, and severe criteria. These procedures—the salpingostomy and fimbrioplasty—are referred to as a neosalpingostomy.^{19,20}

RESULTS

The entire study spans five years, during which participants are monitored via a teleconsultation system to track menstrual patterns and fertile period schedules until pregnancy occurs. A follow-up HSG examination is conducted one month after surgery to confirm that the laparoscopic neosalpingostomy was successful. Once the postoperative HSG confirms that the fallopian tubes are open, the patient is instructed to visit the infertility polyclinic during menstruation to consult with a doctor about a pregnancy plan. If a woman becomes pregnant, it is recorded whether the pregnancy happened naturally or through ovulation induction. Participants are also asked about the time between laparoscopy and pregnancy, gestational age, and pregnancy duration. They are invited to attend the hospital's antenatal care for pregnancy confirmation. Participants who do not become pregnant are encouraged to visit the polyclinic to discuss next steps, including options for pregnancy with assisted reproductive technology. The main outcome is that pregnancy occurs within six months after the HSG confirmation or within seven months following laparoscopic neosalpingostomy. Meanwhile, the live birth rate is the proportion of women who give birth to a live infant, and the ongoing pregnancy rate is the proportion of women with pregnancies extending beyond 24 weeks of gestation. The secondary result is the rate of clinical pregnancy, which is the proportion of

women with an observed fetal heartbeat on ultrasound. Miscarriage is defined as the proportion of women who experience miscarriage before 20 weeks of pregnancy. Abnormal laparoscopic findings and surgery-related complications are also considered. The technique of data analysis involves using univariate, bivariate, and multivariate analysis. Univariate analysis aims to describe each characteristic data. Statistically, data is summarized in terms of standard deviation, or frequency (number of cases), and if necessary, the percentage. Bivariate analysis aims to examine the relationship between two variables in Stata using a chi-square test. Patients' characteristics that meet the proper criteria are outlined in Table 1 and Table 2. There are 72 patients included in the inclusion criteria, but two of them lost follow-up, so the total number of patients in the inclusion criteria is 70, all infertile patients who meet the proper criteria and are then analyzed. No statistically significant association was observed between maternal age >35 years and pregnancy outcomes ($p > 0.05$). Although relative risks suggested a higher trend toward ectopic pregnancy in older patients (RR 2.33), the wide confidence interval (0.42–12.91)

The pregnancy of the both group of patients with the high treatment is 83% happening in the span of 7 months after laparoscopic neosalpingostomy, in which 41 patients are successfully pregnant though without ovulation induction. However, there are only 38 patients who can continue the pregnancy completely, and there are 76% of them deliver the babies using cesarean section due to medical indication.

Similarly, ovulation induction was not significantly associated with improved term pregnancy rates ($p = 1.00$). Although there is no significant difference in table 4 ($p > 0.01$) from 70 patients with infertility due to hydrosalpinx on pregnancy, the relative ratio of age over 35 years old, compared with the ectopic pregnancy, is quite high with a wide range of confidence interval (CI). In multivariate logistic regression analysis, none of the evaluated variables reached statistical significance as independent predictors of term pregnancy ($p > 0.05$). However, maternal age >35 years showed a trend toward reduced likelihood of term pregnancy (AOR 0.74; 95% CI 0.41–1.68). Ovulation induction demonstrated a higher adjusted likelihood of term pregnancy, although not statistically significant (AOR 1.32; 95% CI 0.52–3.01). Meanwhile, in table 5, it seems that the chance in a complete-month pregnancy due to ovulation induction is 0.71% with low range of confidence interval. Ectopic in hydrosalpinx tends to be high with the number of relative risk of 1.43.

DISCUSSION

Infertility caused by fallopian tube phimosis, along with swelling or hydrosalpinx, has been confirmed to damage the embryo through embryotoxic effects and mechanical disruptions in the movement of cilia within the fallopian tube. This condition accounts for 20–30% of cases of female infertility. Laparoscopic neosalpingostomy is reported to be one of the factors causing ectopic pregnancy.^{10–12,21–25} This study finds that 4.1% of the total patient population, although confirmed one month after the procedure through HSG to have patent tubes, still experienced issues. Ectopic pregnancy is also influenced by adhesions that involve not only the fimbria but also other organs in the adnexa. Laparoscopic adhesiolysis is reported to be more effective than laparotomy for both moderate and severe adhesions. No statistically significant link was observed between maternal age over 35 years and pregnancy outcomes ($p > 0.05$). Although the relative risks suggest a higher tendency toward ectopic pregnancy in older women (RR 2.33), the wide confidence interval (0.42–12.91) indicates a lack of statistical precision. Similarly, within the ovulation induction group, there was no significant association with improved term pregnancy rates ($p = 1.00$). Corrective procedures such as peritubal adhesiolysis, fimbrioplasty, and neosalpingostomy performed via laparoscopy remain viable options for patients seeking pregnancy without assistance from assisted reproductive technologies IVF.^{26–30}

Ovulation induction with clomiphene citrate, combined with estradiol valerate, may offer physiological benefits following tubal reconstructive surgery. Clomiphene citrate promotes follicular growth by selectively modulating estrogen receptors, which increases natural gonadotropin release and boosts ovulation frequency. Postoperatively, increased ovulatory events could increase the likelihood of gamete interaction within a newly reconstructed tubal lumen. Additionally, short-term estradiol supplementation might improve endometrial receptivity and support optimal regeneration of the tubal epithelium. Estrogen is important for maintaining ciliary activity and tubal motility, both crucial for transporting the ovum. After surgical trauma, hormonal support may aid mucosal healing and restore fimbrial architecture function. Therefore, although statistical significance was not proven, an 82.8% pregnancy success rate—whether natural or induced ovulation—is observed for up to 7 months following laparoscopic neosalpingostomy in patients with an average infertility duration of

8.2 years. The biological plausibility supports using controlled ovulation induction as an adjunct in selected patients after neosalpingostomy. Compared to previous studies where 60% of pregnancies occurred after fimbrioplasty, this surgical method can be a viable option for patients who desire pregnancy.^{10,11,15}

This study shows that laparoscopic neosalpingostomy in patients with stage III–IV hydrosalpinx results in a relatively high overall pregnancy rate within 7 months after surgery. Although there was no statistically significant difference between the natural conception and ovulation induction groups, a meaningful trend toward higher ongoing pregnancy rates was observed in the induction group. These findings suggest that reconstructive tubal surgery remains a viable fertility-preserving option, especially in settings where assisted reproductive technology (ART) is limited or expensive. The 83% overall pregnancy rate seen in this group is similar to previous reports showing pregnancy rates of 60–70% after fimbrioplasty and neosalpingostomy. The lack of statistically significant differences may be due to the small sample size, which limits statistical power. Still, the observed relative risk patterns indicate potential clinical relevance, warranting further study in larger, multicenter trials.

The 5% incidence of ectopic pregnancy in this study aligns with rates reported after tubal reconstructive surgery. This highlights the need for careful postoperative follow-up and early ultrasound confirmation of intrauterine pregnancy. From a biological standpoint, ovulation induction after neosalpingostomy may boost reproductive success by increasing ovulation frequency and improving endometrial receptivity during early healing. Estrogen supplements might also support tubal epithelial regeneration and ciliary function, thereby enhancing gamete transport.

Clinically, neosalpingostomy could be considered an intermediate step in infertility treatment before IVF, especially for women under 35 with good ovarian reserve and favorable tubal anatomy. However, patients should be counseled about the possibility of needing ART if pregnancy does not occur within 6–12 months.

This study has some limitations. First, the relatively small sample size (n=70) reduces statistical power and may explain the lack of significant differences despite clinical trends. Second, follow-up lasted only 6–7 months; therefore, longer-term reproductive outcomes were not assessed.

CONCLUSIONS

Laparoscopic neosalpingostomy may be considered a fertility-preserving surgical option for women with stage III–IV hydrosalpinx who desire natural conception and decline immediate assisted reproductive technology (ART). In selected patients with preserved ampullary folds and favorable adhesion scores, reconstructive surgery may offer a cost-effective alternative before in vitro fertilization (IVF). Closure of the distal part from the oviduct or fimbriae phimosis is one cause of infertility. The procedure of laparoscopic neosalpingostomy for patients with non-patent HSG and hydrosalpinx damage grade III and IV remains a recommended option before they pursue assisted pregnancy procedures.

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CONFLICTS OF INTEREST

There is no conflict of interest in this study

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Table 1. Classification of Distal tubal Occlusion by Donnez and Casanaz-Roux

No	Degree of damage	Remark
1	Degree I	Phymotic Ostium with preserved tubal patency
2	Degree II	Total Distal Tubal Occlusion Without Ampullary Dilatation
3	Degree III	Ampullary Dilatation inferior to 2.5 cm; ampullary fold well-preserved
4	Degree IV	Hydrosalpinx simple, Dilatation more than 2.5 cm' Well Preserved ampullary fold
5	Degree V	Thick-walled hydrosalpinx; absence of ampullary Folds

Table 2. Characteristics of Patients' Age, Age of Marriage and Maternity

		Total Number	Percentage	Mean
Age	<35	16	27 %	32,5
	>35	56	78 %	38,7
Infertility Age	<5 year	13	18%	3,7

	>5 year	59	82%	8,2
Pregnancy Status	Abortion	16	22 %	
	Ectopic	4	5 %	
	Full Term	38	54 %	
	No Pregnancy	12	17 %	
Maternity Method	Normal Delivery	9	23 %	
	C-Section	29	76 %	
Degree of Hydrosalpinx	Grade III	49	70 %	
	Grade IV	21	30 %	

Table 3. Pregnancy percentage in the span of 7 months after Laparoscopic Neosalpingostomy

	Pregnancy Output									
	abortion		ectopic		Full term		No pregnancy			
	n	%	n	%	n	%	n	%	Total	%
Method of pregnancy										
CC + EE	8	50	1	25	23	60.5	9	75	41	100.0
Natural cycle	8	50	3	75	15	39.4	3	25	29	100.0

CC : Clomiphen Citrat

EE : Estradiol Valerat

Table 4. The Comparison of mothers' age > 35 years old with the pregnancy status

	<i>p</i> Value	RR	CI 95%
Age compared with abortion	0.35	1.53	0.85-2.75
Age compared with ectopic	0.45	2.33	0.42-12.91
Age compared with term pregnancy	0.24	1.29	0.98-1.68

Table 5. The comparison of pregnancy with the ovulation induction

	<i>p</i> Value	RR	CI 95%
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Ovulation Induction compared with abortion	1.00	0.80	0.18-3.53
Ovulation Induction with ectopic	0.25	1.43	0.95-2.14
Ovulation Induction with term pregnancy	1.00	0.71	0.16-3.02

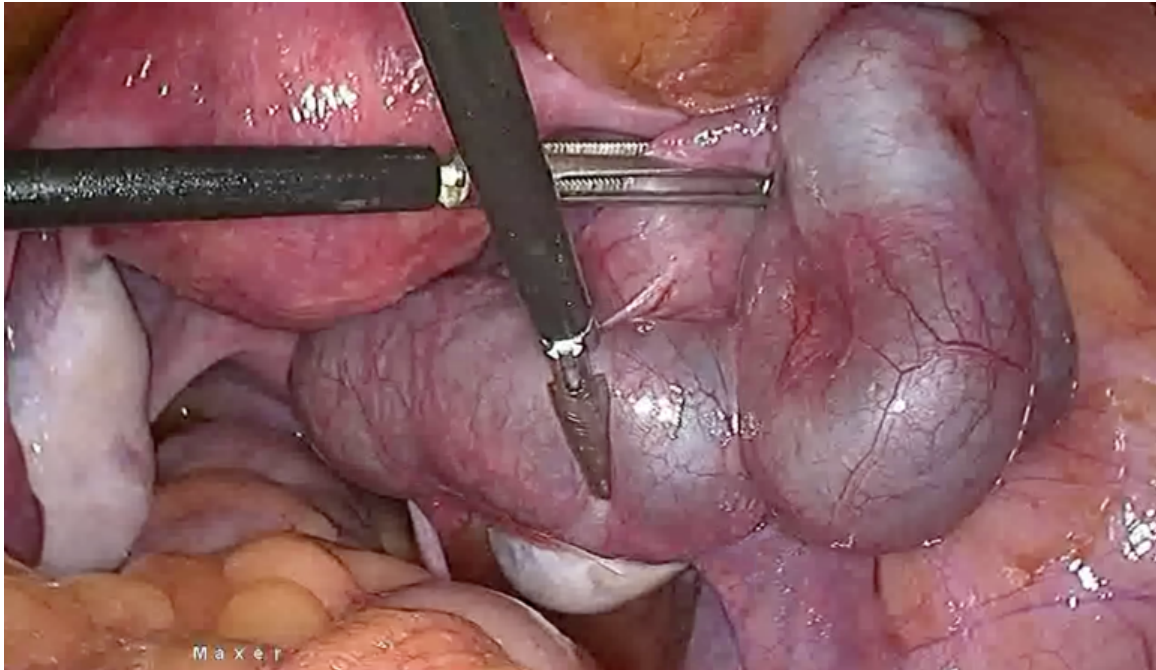


Figure 1. laparoscopic view due to phimosis in both fallopian tubes with damage of grade III and grade IV

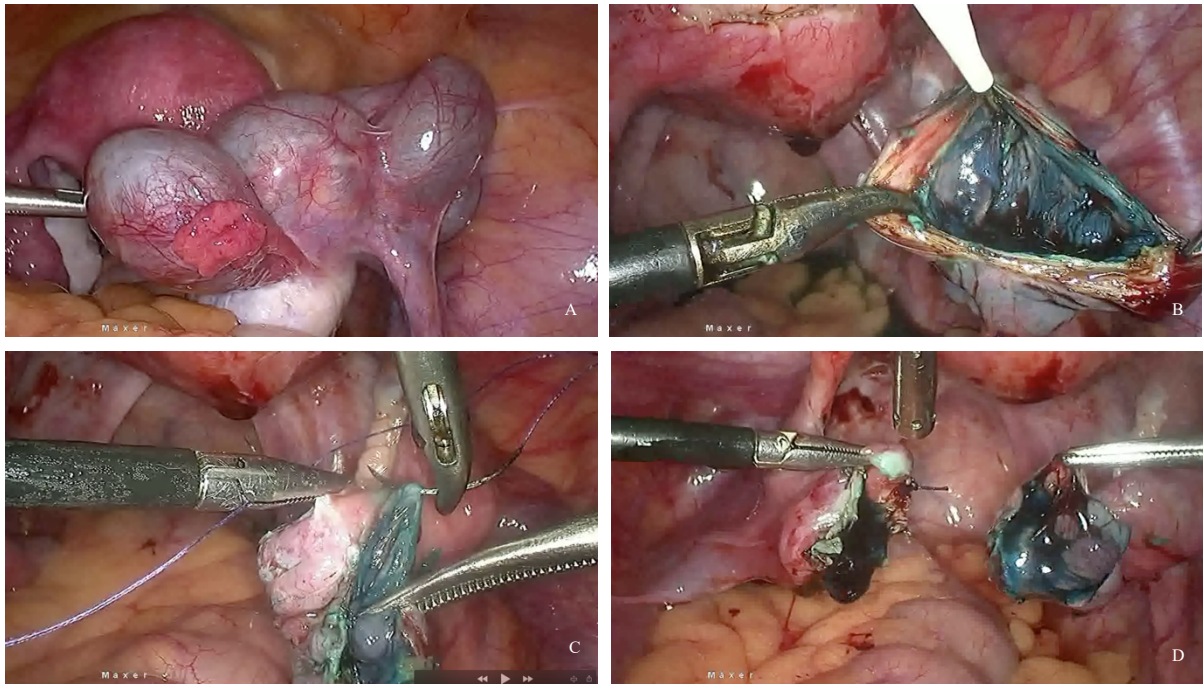


Figure 2. The figure shows picture a in which the distal of fallopian tube is closed (phimosis), the procedure of how the fimbral end opened, laparoscopy neosalpingostomy by stitching the fimbral end and methylene blue dye test to make sure the opened tube.