
بسم الله الرحمن الرحيم
In The Name of ALLAH,

Tubal Factors in Infertility

The fallopian tubes named after Gabriele Falloppio (also spelled Falloppia), a 16th-century physician and surgeon, are appendages of the uterus located on either side at the superior portion of the uterine cavity.

Each tube is divisible into four parts :

proximal narrowest segment , interstitium (1.25 cm long, 1 mm wide) and the isthmus (2.5 cm long, 2.5 mm wide).
The ampulla, the middle segment (5 cm long, 2.5–5 mm wide),gradually widens and merges with the distal segment, the broad funnel-like infundibulum (1.25 cm long, 6 mm wide)of the tubes that lies in close proximity to the ipsilateral ovary.

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CAUSES FOR TUBAL SUBFERTILITY

Tubal congenital anomalies and fallopian tube congenital malformation may be classified into three categories:

1. Total, Partial, or segmented absence
2. Duplication, which can affect ostia and/or the tubes
3. Multiple lumina and diverticula.

Tubal Pathologies and Fertility Outcomes: A Review. 2023.

Developmental or inherent anomalies of the fallopian tubes are rare and most do not require treatment.

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Paraovarian and paratubal cysts

About 10% of adnexal masses consist of paraovarian and paratubal cysts.

These cysts are relatively common, usually asymptomatic, and often discovered incidentally

They are thought to originate from mesothelium or remnants of paramesonephric (Müllerian) and mesonephric (Wolffian) ducts

They may become clinically significant in rare instances due to their size and/or torsion.

Distinguishing between ovarian and paraovarian cysts can be challenging

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The "split" sign, seen on ultrasound ： Separation of a paratubal cyst from the adjacent ovary when pressure is applied in TVS.

Remnants of the paramesonephric duct → hydatids of Morgagni, often develop within the broad ligament instead of at the fimbriated ends of the fallopian tube.

Torsion and large cyst size require more urgent treatment.
Hydatid of Morgagni has been found in over half of patients with unexplained infertility, potentially acting as an obstacle for fimbria in picking up the ovum. Removal of these cysts can improve ovum pick-up and enhance fertility in patients without other causes of infertility ; their surgical resection leads to favorable results on fertility

Tubal Pathologies and Fertility Outcomes: A Review. 2023.

Acquired

Pelvic inflammatory disease (PID) is the most frequent cause for tubal disease of which the single largest cause is *chlamydia trachomatis* infection. Bulk of tubal disease is acquired and may be categorized into—proximal, mid, and distal tubal disease.

Proximal and Mid-tubal Disease

Pathology and blockage of proximal tube account for 10–25% of tubal disease.

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Causes of proximal tubal disease

Pseudo-obstruction	***True anatomic blockage***
Plugs of mucus and amorphous debris	Salpingitis isthmica nodosa
Mucosal agglutination and viscous secretions	Pelvic inflammatory disease
Cornual spasm	Endometriosis
	Cornual polyps
	Intrauterine synechiae

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Salpingitis isthmica nodosa :

Is thought to arise from tubal inflammation of unspecified origin and affects the proximal tube prominently.

Involvement of the distal tube and adhesions in pelvis and perihepatic areas, similar to PID, are also noted.

Laparoscopy shows fibrosed tubal segments. Myosalpingeal hypertrophy encasing endosalpingeal diverticula is noted on histopathological examination.

Pelvic inflammatory disease and endometriosis:

can cause anatomic tubal occlusion by direct involvement or secondary to adhesions.

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Mid-tubal disease is commonly caused by PID, endometriosis, or prior surgery-related inflammations and adhesions that cause steno-occlusions, bulbous termination, scarring, and fibrosis of tubes.

Distal tubal disease includes hydrosalpinges and fimbrial phimosis. Hydrosalpinx is an end stage of distal tubal disease where the distal is completely occluded, whereas a stenosed fimbrial opening due to adhesions results in fimbrial phimosis.

Eighty-five percent of tubal infertility is due to distal tubal disease

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Causes of distal tubal disease

Pelvic inflammatory disease	85% sexually transmitted diseases • *Neisseria gonorrhoeae* • *Chlamydia trachomatis* • *Mycoplasma hominis* • 15% iatrogenic
Tuberculosis	
Peritonitis of any cause	
Tubal damage from previous surgery	
Endometriosis	

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EVALUATION FOR THE TUBAL FACTOR INFERTILITY

When?

Evaluation of the fallopian tube function and patency is a component of the initial triad of diagnostic investigations for infertile couples and is the third in line after evaluation
of semen and ovulation.

Tubal infertility:
should be ruled out in women with history of PID, endometriosis, prior pelvic surgery, or EP.
If tubal pathology is not suspected ⟶ evaluation of tubes is done only if she does not conceive for at least 3 months in spite of satisfactory ovulation and natural or artificial insemination around ovulation.

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Royal College of Obstetricians and Gynaecologists Guidelines for Investigation of Suspected Tubal and Uterine Abnormalities

■ HSG should be offered to women with no suspicion of comorbidities (such as PID, previous ectopic pregnancy, or endometriosis) to screen for tubal occlusion.

■ Where available, hysterosalpingo-contrast-ultrasonography (HyCoSy) screening for tubal patency should be considered because it is an effective alternative to HSG for women who are not known to have comorbidities.

■ When comorbidities are suspected, laparoscopy and chromopertubation should be offered.

■ Do not offer hysteroscopy as part of the initial investigation unless clinically indicated.

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ESHRE Recommendations

ESHRE Capri workshop in 2000 put forward three categories of tests that have established association with healthy pregnancy—semen analysis, tubal patency tests by HSG, or laparoscopy, and tests to detect ovulation.

The ESHRE 2008 guidelines recommend that semen analysis and ovulation assessment before a test of tubal patency is performed.

Women suspected to have comorbidities should be offered laparoscopic assessment directly so that any treatable tubal or pelvic pathology can be evaluated and managed at the same time.

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ASRM Recommendations:

ASRM has suggested specific ruling out of tubal disease by tubal patency tests and chlamydia antibody testing.

Hysterosalpingography, saline infusion sonography (SIS), laparoscopy and chromotubation, and fluoroscopic or hysteroscopic selective tubal cannulation have all been put forward as complementary and not mutually exclusive methods for evaluating tubal patency.

More than one technique is often required for accurate diagnosis and effective treatment of tubal obstruction tests for tubal function.

ULTRASOUND EVALUATION OF FALLOPIAN TUBES

The clinical history and examination in conjunction with the TVS findings decide whether the patient has a high index of suspicion for tubal disease.

The tubal wall is not sonologically discernible unless thickened or distended with fluid.

The distended tubes on ultrasonography (USG) are:

- Thin- or thick-walled (in chronic cases)
- Elongated or folded, tubular, and retort-shaped fluid distended structure
- Separate the uterus and ovary.

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A “cogwheel” appearance from thickened longitudinal folds in a hydrosalpinx when imaged in cross section is pathognomonic of a hydrosalpinx.

Beads on a string” sign is noted when incomplete stations are present.

Atypical hydrosalpinx appearance without any pseudo septation may lead it to be mistaken for an ovarian or paraovarian cyst.

Densely adherent, thick, and multiloculated distended tubes may mimic a complex ovarian tumor.

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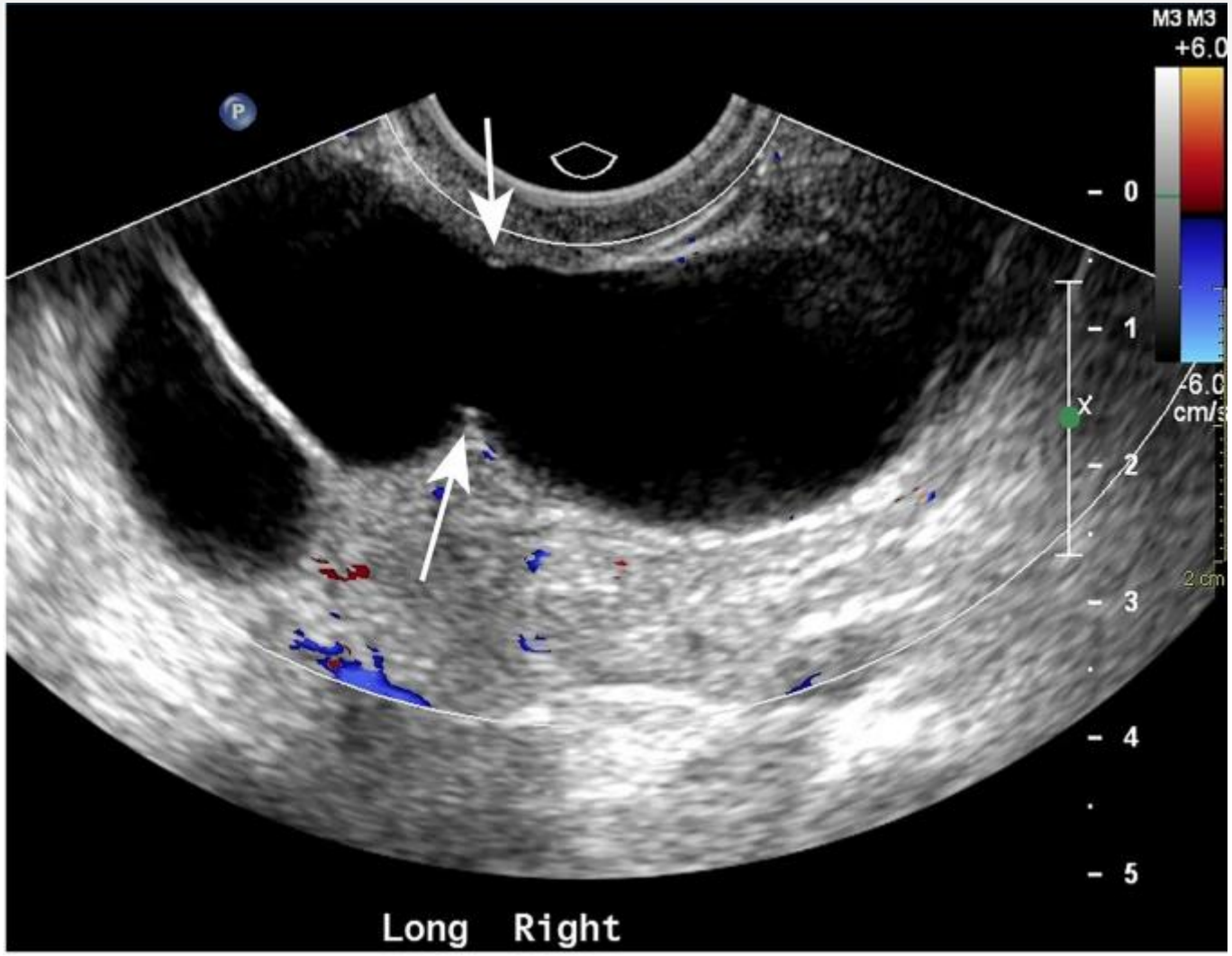
Color Doppler ultrasound image of the right adnexa shows a tubular, avascular, cystic structure with a “waist” (arrows), consistent with a hydrosalpinx



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TUBAL ASSESSMENT TESTS

- Active pelvic infection is an absolute contraindication to performing tubal patency tests.
- There is no single test or symptom that can diagnose salpingitis effectively.
- Even though laparoscopy was considered the gold standard to diagnose salpingitis, almost 20% of PID may show no evidence of salpingitis.
- We should also realize that about 15% of PIDs are iatrogenic with endometrial curettage, biopsy, or HSG.
- Intrauterine contraceptive device insertion being the main causative procedure.

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Centers for Disease Control and Prevention (CDC) criteria to diagnose pelvic inflammatory disease (PID)

Minimum criteria	If one or more of following is present: • Cervical motion tenderness • Uterine tenderness • Adnexal tenderness
Additional criteria	• Oral temperature >101°F (>38.3°C) • Abnormal cervical discharge or cervical friability • Presence of lots of white blood cells on vaginal fluid microscopy • Elevated erythrocyte sedimentation rate • Elevated C-reactive protein • Laboratory confirmation of *Neisseria gonorrhoeae* or *Chlamydia trachomatis* infection
Most specific	• Endometrial biopsy showing endometritis • Transvaginal sonography or magnetic resonance imaging techniques showing thickened, fluid-filled tubes with or without free pelvic fluid or tubo-ovarian complex, or Doppler studies suggesting pelvic infection (e.g., tubal hyperemia) • Laparoscopic findings consistent with PID

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Chlamydial infection is the most common infective cause of tubal disease. The detection of antibodies to C. trachomatis has been associated with tubal pathology.

The meta-analysis by Broeze et al. (2011) evaluated the accuracy of different
chlamydia antibody test (CAT) assays. They found that microimmunofluorescence (MIF) was significantly better than enzyme-linked immunosorbent assay (ELISA) or
immunofluorescence (IF) assays.
Chlamydia antibody test has sensitivity of only 40–50% and positive predictive value (PPV) of 60%, but high negative predictive value (NPV) of 80–90% for detection of distal tubal disease compared to laparoscopy.

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women with low index of suspicion for tubal disease based on history and clinical examination, a negative CAT test reliably rules out the chance of tubal obstruction.

The infection can be treated by treating the couple with a 14–21 day course of doxycycline.

Testing for Tuberculosis

Female genital tuberculosis (FGTB) is an undisputed cause for subfertility.

It causes extensive tubal and endometrial damage. The fallopian tubes are involved in 90–100% cases. Ruling out of TB and curative treatment when diagnosed should be done prior to tube testing, and is ideal in women with : hypomenorrhea, thin endometrium, or features of chronic PID.

FGTB often coexists with other causes of PID like chlamydia and gonorrhea.

Female genital TB diagnosis is challenging as isolation of Mycobacterium tuberculosis by culture which is considered the requisite for diagnosis is often unreliable.

A high index of clinical suspicion and multimodality testing is recommended.

Premenstrual endometrial aspiration or biopsy and PCR allow for rapid diagnosis and help to detect mycobacterial DNA in 80.9% of genital TB-suspected patients.

However, the PCR cannot differentiate between active and latent infection and may be unreliable in identifying the cases that actually require treatment.

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Hence, endometrial sampling and TB stain, BACTEC culture,histopathological examination for tubercles, and diagnostic laparoscopy are used in conjunction with TB PCR to diagnose genital TB.

The new self-contained cassette-based analysis (GeneXpert) is faster than PCR and helps to identify rifampicin-resistant TB also.

TB when diagnosed has to be treated with appropriate antitubercular agents for 9 months.

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Tubal Patency Tests

HSG/HyCoSy are the screening tests that are to be considered for tubal patency evaluation in women with no history/examination suggestive of tubal disease.

In women with or without suspicion of comorbidities that can cause tubal disease and in women with inconclusive or positive screening on HSG/HyCoSy laparoscopy accompanied by hysteroscopy is to be offered as the gold standard for testing tubal integrity.

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Laparoscopy and Chromopertubation

Laparoscopy is the gold standard for diagnosing tubal patency and inflammation.

It allows :

- Diagnosis assessment and management of peritubal disease, adhesions, and endometriosis.
- Biopsy of suspicious lesions for further evaluation.
- Surgical correction of pathology detected, where feasible.

Although laparoscopy is considered the standard, it is not without error as around 3% of patients diagnosed with bilateral tubal block conceive spontaneously.

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Laparoscopic Diagnosis and Grading of Salpingitis

Minimum visual criteria to diagnose salpingitis	• Pronounced tubal surface • Hyperemia • Tubal wall edema • Presence of exudates on tubes and from fimbriae when patent
Mild salpingitis	• Minimum visual criteria, mobile tubes • Patent ostia
Moderate salpingitis	• More evident inflammation, patchy fibrin deposits on tubes • Loose tubal and pelvic adhesions • Tubes not freely mobile
Severe salpingitis	• Intense congestion • Dense adhesions to pelvic structures • Pyosalpinx • Tubo-ovarian masses
Each adnexa should be graded separately	
The overall grade is that of the more severe pathology	

Hysterosalpingography

Hysterosalpingography is an inexpensive and widely available screening test

Cornual tubal spasm is the main reason for lower accuracy of this diagnostic imaging technique.

PID and pregnancy are the two contraindications for performing HSG. Therefore, it is ideally performed in the late follicular phase (day 7–12) following a normal menstrual cycle.

Performing the HSG with an oil-based radiopaque dye has been associated with increased live birth rates. In spite of this, water-based dye is preferred due to better image quality and safety.

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HSG is a reliable indicator of tubal patency if bilateral spill is noted on evaluation.

An abnormal HSG helps predict proximal tubal blockage and hydrosalpinges with moderate accuracy while it is very inaccurate in diagnosing or ruling out distal tubal obstruction and peritubal adhesions. Although an HSG might look normal, hydrosalpinges remain undiagnosed.

Advanced HSG may be done with using fluoroscopic guidance,manipulation, tubal cannulation, and tubal pressure to yield more information and increase reliability of testing.

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Sonohysterosalpingography

SonoHSG is similar to HSG, using ultrasonography and sterile saline instead of fluoroscopy and contrast media, and is another, but less common, method for evaluating tubal factor.

Tubal patency can be observed by the appearance of fluid in the cul-de-sac with the saline infusion,the test does not differentiate between unilateral and bilateral patency.

Hysterosalpingo-contrast sonography

HyCoSy is similar to sonoHSG, but either contrast media or a more recently developed gel comprised of hydroxyethyl cellulose and glycerol is used for demonstrating fallopian tubes.

MANAGEMENT OF TUBAL INFERTILITY

- Preventive approaches
- Identifying and treating pelvic infection/inflammation
- In established tubal disease, management depends on:

- Site and extent of the tubal disease:
  - Unilateral or bilateral
  - Proximal or distal
  - Mild/moderate/severe tubal disease
- Age of the patient
- Duration of fertility
- Ovarian reserve
- Prior fertility
- Presence of other infertility factors
- Experience of the surgeon if tubal surgery is planned
- Success rates of the in vitro fertilization (IVF) program or restorative surgery.

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Prevention of Tubal Infertility

Strategies include:

1) General education and awareness to decrease the incidence of sexually transmitted infection (STI) and PID

2) Proper precautions to reduce the incidence of iatrogenic PID/peritubal adhesions

3) Early identification and treatment of STI and PID and treatment of the partners

4) Identifying patients with unfavorable reproductive microbiome and optimizing their health to reduce the risk of infections.

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Reproductive Tract Microbiome

Women undergoing IVF with tubal factor infertility (a pathology associated with infections) were found to be more likely to have a vaginal microbiota consistent with bacterial vaginosis (BV) by analysis of smears.

Studies have shown that presence of unfavorable non-lactobacillus dominant
microbiomes are significantly more in infertile women.

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Distal Tubal Obstruction

Distal tubal occlusive disease exhibits a wide spectrum of severity ranging from adherent fimbrial folds to varying degrees of phimosis, to complete obstruction with hydrosalpinges.

Fimbriolysis refers to the separation of adherent fimbria, fimbrioplasty describes the correction of phimotic but patent fimbria, and neosalpingostomy involves the reopening of a completely obstructed tube.

The extent and character of associated tubo-ovarian adhesions, the tubal thickness, and the condition of the internal ampullary mucosal architecture are all variables that affect prognosis.

For the milder forms of distal tubal disease, postoperative live birth rates can exceed 50%.

Results achieved with surgery for more severe disease have varied widely, but success rates are lower (10–35%) and risk for ectopic pregnancy is higher (5–20%).

Postoperative tubal patency rates far exceed pregnancy rates;patency is more easily restored than function because mucosal regeneration is slow and often fails altogether.

The majority of pregnancies occur within the first 2 years after surgical treatment of distal tubal obstruction.

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In a case series of 35 women with distal tubal occlusion treated by laparoscopic fimbrioplasty followed for at least 2 years after surgery:

- ✓ Global conception rate was 74%
- ✓ Intrauterine pregnancy rate was 51%
- ✓ live birth rate was 37%
- ✓ EP was 23%.

In younger women with mild distal tubal occlusive disease, laparoscopic surgery may be viewed as an alternative to IVF, but when disease is severe or pregnancy does not occur during the first postoperative year, IVF is the logical choice.

For older women with any degree of distal tubal disease, IVF is the first and best option because cycle fecundability after distal tubal surgery is low (1–2%), time is limited, and IVF is both more efficient and more effective.

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In the presence of hydrosalpinges:

- ✓ Pregnancy, implantation, and delivery rates are decreas 50%
- ✓ Abortion rates are increased

Several mechanisms have been implicated to explain :

- ✓ mechanical interference with implantation

  Toxic effects on the embryo or endometrium.

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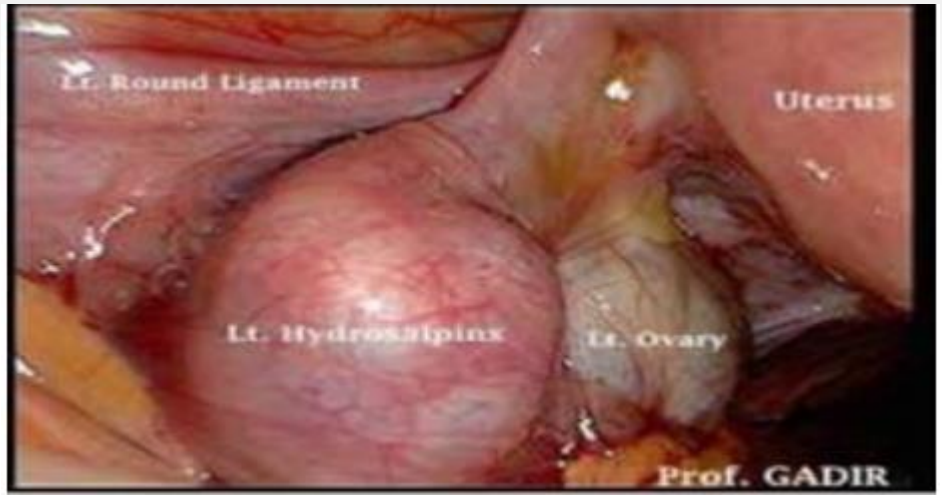
A 2010 systematic review including five RCT involving 646 women observed that the odds of achieving anongoing pregnancy were twice as great after laparoscopic salpingectomy for hydrosalpinges before IVF (OR = 2.14, CI = 1.23–3.73).
Laparoscopic occlusion of the fallopian tubes increased the odds of clinical pregnancy, compared to no intervention (OR = 4.66, CI = 2.47–10.01), and neither surgical procedure was superior.



These data demonstrate clearly that laparoscopic salpingectomy or tubal occlusion improves IVF pregnancy rates in women with hydrosalpinges.

This holds true even when only one tube is affected. Moreover, removal or proximal occlusion of unilateral hydrosalpinx seems to improve chances of spontaneous pregnancy.

A retrospective series including 25 women with unilateral hydrosalpinx reported 88% pregnancy rate without IVF with an average time to pregnancy of 5.6 months.

Despite contradictory results in early reports, salpingectomy does not impact ovarian reserve, perhaps except when it is done for ectopic pregnancy.

Ovarian stimulation parameters and implantation and clinical pregnancy rates are similar in women who underwent salpingectomy or laparoscopic proximal tubal occlusion.

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Ultrasound-guided aspiration of hydrosalpingeal fluid at the time of oocyte retrieval has been suggested as an alternative treatment.

The procedure is effective in improving IVF outcome as compared to no intervention, simpler, and less costly than surgical options.

However, salpingectomy and proximal tubal occlusion fare better than fluid aspiration with regard to ongoing pregnancy, clinical pregnancy, ectopic
pregnancy, and miscarriage rates.

Moreover, the fluid reaccumulates rapidly

Aspiration of hydrosalpingeal fluid can be an option reserved for women who are likely to have severe intra-abdominal adhesions prone to complications with pelvic surgery.

Essure (2-mm-thick and 4-cm-long)inserts have been used for occlusion of
hydrosalpinges prior to IVF. Hysteroscopic placement of Essure coils are relatively easy; however, clinical pregnancy, implantation, and live birth rates following Essure are significantly lower than those achieved with laparoscopic management (salpingectomy or proximal occlusion) of hydrosalpinges.

Some evidence suggest that miscarriage rate is higher following Essure blockage of hydrosalpinges, as compared with other interventions.

Similar to hydrosalpinx aspiration, currently,Essure can be regarded as a second-line intervention for women under high risk of intra-abdominal adhesions.

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Proximal Tubal Obstruction

Proximal tubal occlusions represent 10–25% of all tubal obstructions observed with HSG, many of which are not real (20–40%).

Mucus plugs, cellular debris, or uterotubal spasm can cause pseudo proximal obstruction.

Repeated HSG can decrease the number of false-positive tests of tubal patency

in a case series including 98 infertile women with a diagnosis of proximal tubal occlusion based on an HSG, repeating the procedure revealed bilateral tubal patency in 14 patients (14%), patency of 1 tube in 12 others (12%), and confirmed bilateral occlusion in 72 patients (74%).

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If proximal occlusion is not due to SIN, tubal cannulation using hysteroscopic or fluoroscopic methods is a proven alternative to traditional microsurgical repair.

Clinical pregnancy rate following tubal catheterization for unilateral or bilateral proximal tubal occlusion was 27% (95% CI =25–30%).
The pooled live birth and ectopic pregnancy rates were 22% (95% CI = 18–26%) and 4% (95% CI 3–5%), respectively.

A 2017 systematic review and meta-analysis pooled 27 studies involving women with proximal tubal occlusion.

Pregnancy rates were not significantly different between tubal catheterization with hysteroscopic, laparoscopic, or fluoroscopic guidance (31% vs. 26%, respectively).

Reocclusion rate of the opened tubes was approximately 30%.

Selective salpingography with catheterization immediately after HSG shows proximal occlusion can be an appropriate next step since it saves time for both physician and patient.

Microsurgical segmental tubal resection and anastomosis are a proven treatment For true proximal tubal obstruction. Experienced surgeons can achieve pregnancy rates ranging between 50% and 60%.

But the number of surgeons having the necessary expertise is fast declining. Outcomes vary with the cause of the obstruction; reocclusion rates are relatively high with causes other than SIN.

Bipolar tubal disease involves both proximal and distal tubal obstructions.
Success rates with surgery have been extremely poor and IVF represents the best treatment option.
When cannulation fails, microsurgery may be considered if IVF is not an option.

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با تشکر از توجه شما