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# The impact of ovarian surgery on female fertility: The mediating role of reduced ovarian reserve

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**Abstract**

Ovarian surgery, including oophorectomy and cystectomy, harms female fertility by reducing ovarian reserve. Anti-Müllerian Hormone (AMH) and Antral Follicle Count (AFC) are proper ovarian function biomarkers. The aim of the study was to investigate the impact of ovarian surgery on female fertility and determine if reduced ovarian reserve is a mediator of this impact. An analytical case–control study was conducted among 230 women (115 cases, 115 controls) aged 18–40 years at the Gynecology and Obstetrics Teaching Hospital, Babylon, Iraq. Cases were those with a history of ovarian surgery; controls were age- and parity-matched. Sociodemographic, reproductive, and surgical data were determined by questionnaire and clinical record. AMH and AFC were measured by ELISA and transvaginal ultrasonography, respectively. Multivariable logistic regression and Structural Equation Modeling (SEM) assessed association and mediation. : Women with ovarian surgery had decreased AMH (1.72 ± 0.84 vs. 2.89 ± 0.91 ng/mL, $p < 0.001$) and AFC (7.6 ± 3.1 vs. 11.8 ± 3.8, $p < 0.001$). Surgery was associated with lower rates of spontaneous conception (24.3% vs. 47.0%, $p < 0.001$) and increased use of ART (54.8% vs. 29.6%, $p < 0.001$). SEM identified that diminished ovarian reserve mediated 53.6% of the effect of surgery on infertility. Ovarian surgery profoundly harms fertility, primarily via compromised ovarian reserve. Preoperative counseling, fertility-conserving surgical approaches, and post-operative assessment of ovarian reserve are strongly advocated, particularly in endometriosis or a history of ovarian surgery. Referral for assisted reproduction should be considered early.

**Keywords:** Ovarian surgery, Fertility, Ovarian reserve, AMH, Antral follicle count

## Introduction

The impact of ovarian surgery on the fertility of women has been of great clinical and research interest, that is, its impact on ovarian reserve. Ovarian surgery in the form of cystectomy, oophorectomy, and ovarian drilling is generally performed to manage benign ovarian cysts, endometriomas, and PCOS [1,2]. While these therapies are intended to alleviate symptoms and promote reproductive success, they have been found to actually detract from ovarian reserve, thereby having a detrimental effect on fertility potential [3,4]. Ovarian reserve, i.e., the quantity and quality of a woman's residual oocytes, is a predictor of reproductive potential and is commonly assessed through biomarkers such as Anti-Müllerian Hormone (AMH) levels and antral follicle count (AFC) [5,6]. Several studies have demonstrated that ovarian surgery, particularly endometrioma excision, can lead to substantial declines in ovarian reserve [7]. Postoperative AMH levels have declined with bilateral surgery leading to reductions up to 44% [8]. Laparoscopic cystectomy for benign ovarian cysts has also been associated with low AFC [9] and reduced ovarian responsiveness in ART [10]. These findings confirm that even when surgery is clinically indicated, it will have unexpected consequences for the future fertility, and hence there is a requirement for careful surgical planning and preservation of fertility. The mediating effect of lowered ovarian reserve between ovarian surgery and fecundity has increasingly emerged. Studies show that the ovarian reserve may recover to some extent with time after surgery [11], whereas others document long-term depletion, particularly for procedures with severe tissue loss or bilateral procedures [12,13]. Second, surgical technique, such as the method of hemostasis (electrocoagulation versus suturing), also appears to influence the degree of ovarian impairment, with more pronounced reductions seen with electrocoagulation [14]. Such results make a case for

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careful consideration of both indication and surgical technique as a way of minimizing long-term risk to fertility. Therefore, the current research seeks to provide an in-depth explanation of how ovarian surgery influences female fertility through the mediating role of reduced ovarian reserve.

## Material and Methods

### Study design

This study employed an analytical case–control design to quantify the impact of ovarian surgery on female fertility and to explore the mediating influence of reduced ovarian reserve. Case–control design was employed because it is suitable for the investigation of associations between exposure and outcome, and is efficient in assessing of relatively rare exposures such as ovarian surgery. Women who had previously undergone ovarian surgery were labeled as cases, whereas those without pre-existing ovarian surgery were used as controls. Age and parity were employed as matching variables to reduce possible confounding.

### Study sitting and duration

The research was conducted at the Babylon Governorate Gynecology and Obstetrics Teaching Hospital and its outpatient clinics attached to it in Iraq. The hospitals are the major referral for gynecology and infertility services within the region, with access to a heterogeneous patient population. Data was collected from January 2025 to August 2025, for 8 months, in order to allow sufficient time to recruit participants, perform laboratory tests, and verify data.

### Study population

The study population comprised women of childbearing age (18–40 years) who attended the study sites for gynecological evaluation, infertility workup, or surgical intervention. Two participant groups were recruited:

Cases–those who had previously undergone ovarian surgery, including cystectomy, unilateral or bilateral oophorectomy, or excision of endometriomas.

Controls–women with no previous history of ovarian surgery, matched to the cases by parity and age (±2 years).

### Sample size determination

Sample size was determined based on G*Power program for case–control studies. Assuming a medium effect size of 0.35, significance of 0.05, and power of 80%, there needed to be at least 100 participants per group. The sample was escalated by 15% to accommodate possible non-response or missing data. Thus, a total of 230 women were finally included in the study (115 cases and 115 controls). This sample population was in line with other international studies of ovarian reserve following gynecologic surgery [15].

### Inclusion and exclusion criteria

The inclusion criteria were: women between 18–40 years of age, with normal menstrual cycles (21–35 days), and providing informed consent to participate in the study. The exclusion criteria were: women who have received chemotherapy, radiotherapy, or pelvic irradiation; individuals with premature ovarian insufficiency or other systemic endocrine diseases (e.g., thyroid disease, hyperprolactinemia); women with a history of hysterectomy or bilateral oophorectomy; and individuals who refuse to participate.

### Study instruments

Data were collected by a standardized interviewer-administered questionnaire, abstraction of medical records, and laboratory testing. The questionnaire gathered sociodemographic data, reproductive history, lifestyle factors (e.g., smoking and BMI), and gynecologic history. Surgical and clinical data such as side, type, and extent of ovarian surgery were ascertained from operative reports. Ovarian reserve was ascertained via two validated markers:

Serum level of anti-Müllerian Hormone (AMH) in ng/mL by Enzyme-Linked Immunosorbent Assay (ELISA). AMH was chosen as it is cycle-independent and a good measure of the ovaries' reserve [16].

Antral Follicle Count (AFC), quantified by transvaginal ultrasonography on menstrual cycle days 2–4 by an experienced gynecologist to satisfy standardization and reduce inter-observer variation [17].

### Sample collection procedure

A 5 mL venous blood sample was collected in the early follicular phase (day 2–4 of menstruation). The samples were centrifuged, and aliquots of serum were stored at −20°C until they were analyzed. AMH was approximated with a standard ELISA kit. At the same phase of the cycle, transvaginal ultrasonography was performed utilizing a high-frequency probe in order to determine AFC. All laboratory work was following the manufacturer's instructions, and quality control procedures were followed.

### Ethical considerations

The protocol for the study was approved by the Institutional Review Board (IRB) of the College of Medicine, University of Babylon. Written informed consent was obtained from all participants after a clear description of study aim and methodology. Data anonymity and confidentiality were maintained by anonymizing data, and records were kept accessible only to the research team.

### Statistical analysis

Data were processed using SPSS version 29 and AMOS 29 for structural equation modeling. Descriptive statistics were presented as mean ± standard deviation for continuous variables and frequencies and percentages for categorical variables. Independent t-tests or Mann–Whitney U tests were applied to compare continuous variables between controls and cases, and chi-square tests for comparing categorical variables. Analysis of covariance (ANCOVA) was conducted to adjust for potential confounders such as age, BMI, and duration of infertility when comparing markers of ovarian reserve among surgical subgroups. Effect sizes were estimated using Cohen's d to determine the magnitude of differences between groups. Relative risks (RR) and 95% confidence intervals were estimated to compare fertility outcomes, and multivariable logistic regression was performed to identify independent predictors of infertility, with adjusted Odds Ratios (OR) and 95% CIs reported. Finally, Structural Equation Modeling (SEM) was performed to ascertain whether reduced ovarian reserve mediated the relationship between ovarian surgery and infertility, with model fit being entertained using CFI, RMSEA, and SRMR indices. Statistical significance was established at $p < 0.05$.

## Results

the baseline sociodemographic and clinical characteristics of the 230 women enrolled into the study as presented in Table 1. The two groups were matched for age, parity, education, and employment status, as expected by the strength of the case–control design. There was no statistically significant difference in mean age (31.2 vs. 30.9 years, $p = 0.61$) or parity distribution ($p = 0.89$). However, women with a history of ovarian surgery had a significantly longer mean duration of infertility compared to controls (3.9 ± 2.2 vs. 2.6 ± 1.8 years, $p < 0.001$). Although the case group also had a trend towards higher BMI, comparison was not significant statistically ($p = 0.08$). The SMD were predominantly small (<0.25), confirming minimal imbalance at baseline with the exception of infertility duration.

**Table 1.** Baseline characteristics of the study population (n=230)

| Variable | Cases (n=115) | Controls (n=115) | SMD | p-value |
|---|---|---|---|---|
| Age (years, mean ±SD) | 31.2±4.8 | 30.9 ± 4.6 | 0.06 | 0.61 |
| BMI (kg/m$^2$, mean ±SD) | 26.7 ± 3.9 | 25.8 ± 3.6 | 0.24 | 0.08 |
| Smoking (%) | 18.3 | 13.0 | 0.14 | 0.29 |
| Duration of infertility (years, mean ± SD) | 3.9 ± 2.2 | 2.6 ± 1.8 | 0.63 | <0.001* |
| Education ≥ Secondary (%) | 68.7 | 72.2 | 0.08 | 0.57 |
| Employment (%) | 40.0 | 43.5 | 0.07 | 0.63 |

The surgical and gynecologic profiles of the case group women. Ovarian cystectomy (50.4%) was the most common operation done, followed by excision of endometrioma (29.6%) and unilateral oophorectomy (15.7%). Bilateral partial oophorectomy was less frequent (4.3%) Table (2) below shows Table 2. There was clear gradient present between the extent of surgery and ovarian reserve markers: those who underwent more extensive procedures (particularly bilateral procedures) had lower mean AMH and AFC levels in comparison to cystectomy cases. ANCOVA analysis, adjusted for age, BMI, and infertility duration, confirmed that both type and laterality of surgery were independently associated with diminished ovarian reserve (p-trend < 0.001).

**Table 2.** Surgical characteristics of the case group (n=230)

| Surgical Variable | Frequency (%) | Mean AMH (ng/mL) | Mean AFC | P-trend |
|---|---|---|---|---|
| Type of Surgery | | | | |
| Cystectomy | 50.4 | 1.96 ± 0.77 | 8.2 ± 3.0 | — |
| Endometrioma excision | 29.6 | 1.48 ± 0.62 | 6.8 ± 2.9 | 0.02* |
| Unilateral Oophorectomy | 15.7 | 1.22 ± 0.55 | 5.9 ± 2.5 | <0.001* |
| Bilateral partial Oophorectomy | 4.3 | 0.94 ± 0.42 | 4.7 ± 2.1 | <0.001* |
| Laterality | | | | |
| Unilateral | 83.5 | 1.78 ± 0.79 | 7.9 ± 3.2 | — |
| Bilateral | 16.5 | 1.14 ± 0.61 | 5.5 ± 2.8 | <0.001* |

*ANCOVA adjusted for age, BMI, and infertility duration

Ovarian reserve was lower in women with a history of ovarian surgery compared to controls. The mean level of AMH was appreciably lower in the case group (1.72 ± 0.84 vs. 2.89 ± 0.91 ng/mL, adjusted mean difference = −1.11, 95% CI −1.36 to −0.86, p < 0.001). The mean antral follicle count was also appreciably lower in cases (7.6 ± 3.1 vs. 11.8 ± 3.8, p < 0.001). Substantial group differences were identified from estimates of effect sizes (Cohen's d > 1.0 for AFC and AMH), illustrating the extreme adverse impact of ovarian surgery on markers of reproductive capacity even after controlling for confounders, Table 3.

**Table 3.** Ovarian reserve markers in cases vs controls (Adjusted Analysis)

| Marker | Cases (n=115) | Controls (n=115) | Adjusted Mean Difference (95% CI) | Cohen's d | P-value |
|---|---|---|---|---|---|
| AMH (ng/mL) | 1.72 ± 0.84 | 2.89 ± 0.91 | −1.11 (−1.36, −0.86) | 1.29 | <0.001* |
| AFC | 7.6 ± 3.1 | 11.8 ± 3.8 | −4.2 (−5.3, −3.1) | 1.18 | <0.001* |

*ANCOVA adjusted for age, BMI, smoking, and infertility duration.

Women who had previous ovarian surgery had significantly lower spontaneous conception rates at 12 months (24.3% vs. 47.0%, RR = 0.52, p < 0.001) and higher utilization of assisted reproductive technology (ART) to achieve conception (54.8% vs. 29.6%, RR = 1.85, p < 0.001). While miscarriage was more common in cases (16.5% vs. 9.6%), this was not statistically significant (p = 0.12). Kaplan–Meier analysis for time-to-pregnancy also emphasized such differences, with cases having much longer median time-to-conception (16 months compared to 9 months, log-rank p < 0.001). Combined, these findings demonstrate that ovarian surgery compromises natural fertility potential and delays reproductive success, Table 4.

**Table 4.** Fertility outcomes by study group

| Outcome | Cases (n=115) | Controls (n=115) | RR (95% CI) | P-value |
|---|---|---|---|---|
| Spontaneous conception within 12 months (%) | 24.3 | 47.0 | 0.52 (0.36–0.74) | <0.001* |
| Requirement of ART (%) | 54.8 | 29.6 | 1.85 (1.34–2.56) | <0.001* |
| Miscarriage rate (%) | 16.5 | 9.6 | 1.72 (0.84–3.49) | 0.12 |
| Median time-to-pregnancy (months, Kaplan–Meier) | 16 (95% CI: 13–19) | 9 (95% CI: 7–12) | — | <0.001* |

The multivariable logistic regression model, Table 5, reasserted ovarian surgery as a strong independent predictor of infertility (adjusted OR = 2.34, 95% CI 1.45–3.77, $p < 0.001$). Low ovarian reserve, defined by low AMH (<1.5 ng/mL) and reduced AFC (<8), also highly predicted infertility with odds ratio of 3.12 and 2.79, respectively. Age >35 years and obesity (BMI >30 $kg/m^2$) correlated with increased risk of infertility but failed to reach statistical significance. Of note, an interaction effect was found between ovarian surgery and endometriosis, indicating a synergistic effect on fertility outcome (OR = 1.91, p = 0.04). The regression model had high discriminatory capacity (AUC = 0.84, 95% CI 0.78–0.89) and good calibration (Hosmer–Lemeshow p = 0.62), and this confirms the consistency of the predictive estimates.

**Table (5):** Multivariable logistic regression for infertility

| Predictor | Adjusted OR | 95% CI | P-value |
|---|---|---|---|
| Ovarian surgery (Yes vs. No) | 2.34 | 1.45–3.77 | <0.001* |
| Low AMH (<1.5 ng/mL) | 3.12 | 1.82–5.33 | <0.001* |
| Low AFC (<8) | 2.79 | 1.66–4.71 | <0.001* |
| Age > 35 years | 1.65 | 0.91–3.01 | 0.10 |
| BMI > 30 $kg/m^2$ | 1.38 | 0.72–2.64 | 0.32 |
| Interaction: Surgery × Endometriosis | 1.91 | 1.02–3.58 | 0.04* |

Model fit indices: Hosmer–Lemeshow p = 0.62; AUC = 0.84 (95% CI: 0.78–0.89).

Structural Equation Modeling (SEM) was employed to test whether reduced ovarian reserve mediated the relationship between ovarian surgery and infertility, Table 6. Overall impact of ovarian surgery on infertility was significant ($\beta = 0.84$, $p < 0.001$). Operation was significantly associated with low AMH ($\beta = -0.62$, $p < 0.001$) and low AFC ($\beta = -0.54$, $p < 0.001$), and these were significant predictors of infertility. The indirect effect through these markers of ovarian reserve accounted for 53.6% of the total effect, supporting partial mediation. The direct relationship between surgery and infertility remained significant but was attenuated ($\beta = 0.39$, p = 0.04), indicating that reduced ovarian reserve is an important explanatory pathway. The SEM model demonstrated excellent fit indices (CFI = 0.97, RMSEA = 0.04, SRMR = 0.03), validating the proposed mediation model.

**Table (6):** Structural Equation Modeling (SEM) for mediation pathways

| Pathway | β (SE) | 95% CI | p-value |
|---|---|---|---|
| Surgery →Infertility (total effect) | 0.84 (0.21) | 0.43–1.25 | <0.001* |
| Surgery →Reduced AMH | −0.62 (0.11) | −0.84 to −0.40 | <0.001* |
| Surgery →Reduced AFC | −0.54 (0.13) | −0.79 to −0.29 | <0.001* |
| AMH →Infertility | 0.41 (0.10) | 0.21–0.61 | <0.001* |
| AFC →Infertility | 0.33 (0.09) | 0.15–0.51 | 0.001* |
| Direct effect (surgery → infertility) | 0.39 (0.19) | 0.02–0.76 | 0.04* |
| Indirect effect (mediated by AMH+ AFC) | 0.45 (0.14) | 0.21–0.69 | 0.001* |
| Proportion mediated | 53.6% | — | — |

SEM model fit indices: $\chi^2/df = 1.21$; CFI = 0.97; RMSEA = 0.04; SRMR = 0.03.

## Discussion

Baseline comparison confirmed that the two groups were evenly matched on demographic and clinical factors, maintaining the case–control design. The groups were not different in terms of age, parity, education, or employment status and thereby reducing confounding in future analysis. However, women with a history of previous ovarian surgery had significantly longer duration of infertility compared to controls. This finding is clinically significant, as greater infertility duration per se is associated with reduced fecundability and poorer outcomes following assisted reproductive technologies [18,30]. The trend for greater BMI in cases of surgery might also have contributed to fertility issues, given the established impact of obesity on ovulatory function and reproductive endocrinology. These baseline findings revealed that while the groups were similar on all factors, the increased burden of infertility in the surgical cases necessitated closer evaluation of markers of ovarian reserve as a possible mediator.

Stratification of surgical factors revealed a clear dose–response relation between the extent of ovarian surgery and diminished ovarian reserve. Females undergoing more extensive surgeries, such as unilateral or bilateral oophorectomy, had significantly lower AMH and AFC compared to cystectomy cases. This gradient indicates the detrimental impact of surgery-induced loss of intact ovarian tissue either through mechanical disruption or through thermal damage during surgery. Other studies have also shown that endometrioma resection and repeated ovarian surgery are particularly harmful to ovarian reserve, reducing both AMH levels and subsequent reproductive capacity [19,20]. In addition, the laterality effect noted in this study is in line with earlier evidence showing that bilateral procedures accelerate the decline in ovarian reserve and can result in premature ovarian failure [21]. These observations highlight the importance of surgical restraint and fertility-sparing techniques in gynecologic surgery.

The comparison between groups of ovarian reserve markers indicated that women who had a history of ovarian surgery had significantly lower levels of AMH and AFC counts with large effect sizes even after adjustment for confounders. This provides strong evidence that ovarian surgery is strongly associated with decreased ovarian reserve. Both AMH and AFC are thought to be established predictors of reproductive life and outcome in assisted reproduction [1]. Decreased in this research is clinically relevant, as a drop in AMH reflects primordial follicle pool depletion, while decreased AFC indicates reduced immediate ovarian responsiveness to gonadotropins. Consistent with evidence, meta-analyses found consistent evidence that ovarian cystectomy and endometrioma resection significantly reduce ovarian reserve biomarkers, particularly when some healthy ovarian tissue is incidentally removed [22]. This highlights the biological validity of impairment of fertility after surgery through a process of follicular pool exhaustion.

Fertility histories revealed that women with a history of ovarian surgery had decreased rates of spontaneous conception and were at higher risk of requiring ART for pregnancy attainment. Their median time-to-pregnancy was also significantly longer than in controls, confirming clinically significant prolongation in reproductive success. Although there were higher rates of miscarriage in the surgical group too, this did not reach statistical significance and suggests that the primary mechanism of reduced fertility is impaired conception and not lost pregnancy. These results are consistent with previous cohort studies that established lower natural conception rates following ovarian surgery, particularly among women having bilateral surgery or endometriomas [23]. Furthermore, a prospective study revealed that time-to-pregnancy almost doubled in women who had previously had ovarian surgery, which was in line with findings herein [24]. Collectively, these findings underscore the value of initiating early fertility counseling and discussion of ART in women with surgical history.

The multivariable logistic regression model validated ovarian surgery as an independent predictor of infertility after controlling for confounding factors such as age, BMI, and ovarian reserve. Of particular interest, low AMH and low AFC were the strongest predictors and confirmed their leading role as biomarkers linking surgical exposure to reproductive outcomes [25]. The interaction that was seen between endometrioma surgery and endometriosis suggests that women who are being operated upon because of endometrioma may have an exacerbating risk, as both disease and treatment were adverse to ovarian function. Prior evidence indicates that endometriosis itself affects ovarian reserve by promoting fibrosis and local inflammation, and in conjunction with surgery, the synergistic effect on fertility further destroys it [26]. The predictive accuracy of the model (AUC = 0.84) was outstanding and emphasizes its clinical use for risk stratification. These findings strengthen the role of individualized patient assessment while making surgical plans in women who desire to maintain future fertility [27].

SEM mediation analysis gave mechanistic insight and showed that over half of the impact of ovarian surgery on infertility was mediated by decreased AMH and AFC. This partial mediation shows that although decreased ovarian reserve accounts for much of the fertility compromise, other pathways, e.g., disrupted ovarian blood flow, adhesions from surgery, or pelvic anatomical changes are possible. The robust indirect effect through ovarian reserve is consistent with prior mechanistic study evidence of follicular loss and stromal damage as direct outcomes of ovarian surgery [28]. Another longitudinal study published more recently also demonstrated that declines in AMH post-surgery mediated the association between excision of endometrioma and reduced live birth in ART cycles [29]. The SEM model's high fit indices provide further support to this mediational pathway. These findings highlight reduced ovarian reserve as a key mechanism through which surgery is linked to infertility and reassert the clinical importance of preoperative counseling, ovarian reserve testing, and fertility-sparing strategies.

## Study limitations

This research has several limitations that should be mentioned. First, causal inference is not possible with the case–control design, and residual confounding owing to unmeasured influences, such as subtle genetic or lifestyle factors, cannot be excluded. Second, the sample was from one geographic region, and the generalizability of the results to other populations therefore may be limited. Third, although AMH and AFC are helpful indicators of ovarian reserve, they are indirect and may not fully represent functional fertility potential. Finally, long-term reproductive outcomes, i.e., live birth rates, were not evaluated in the study, which would have provided additional information on the clinical significance of surgery-related ovarian reserve loss.

## Conclusion

The findings of this study demonstrate that ovarian surgery, particularly bilateral or extensive, drastically reduces ovarian reserve as evidenced by reduced AMH levels and AFC and significantly impairs female fertility, with increased time-to-pregnancy and increased requirement for assisted reproductive technologies. Reduced ovarian reserve mediates over half of the surgical impact on infertility, pointing to its central role as a mechanistic pathway. Clinically, these observations underscore the need for preoperative fertility counseling for women in the reproductive age group, careful surgical planning to minimize the removal of normal ovarian tissue, consideration of fertility-sparing options (e.g., drainage of cysts or limited excision), and routine assessment of ovarian reserve preoperatively and postoperatively. In addition, the women having risk factors such as endometriosis or prior ovarian surgery must be under strict surveillance, and early referral to reproductive specialists is recommended for the optimization of the reproductive outcomes and planning regarding the use of assisted reproduction or fertility preservation strategies.

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## Conflicts of interest

There are no conflicts of interest.

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