

A Case-Control Study to Assess the Risk Factors of Ectopic Pregnancy in Two Referral Hospitals in Douala, Sub-Saharan Africa

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Abstract

Background: Ectopic pregnancy (EP) remains a public health problem in Africa, with a prevalence of 1% - 4% of all pregnancies and a main contributor to the high maternal mortality rates. This study aimed to identify and quantify the risk factors associated with EP in two major referral hospitals in Douala, thereby informing strategies for improved prevention and management. **Methods:** A retrospective case-control study was conducted over five months, from February 1 to June 30, 2023, at the Douala General Hospital and the Gynaeco-Obstetric and Pediatric Hospital of Douala. Medical records of patients managed for EP between January 1, 2013, and December 31, 2022, were reviewed. Cases (EP) were compared with controls (intrauterine pregnancy, (IUP) in a 1:2 ratio, matched for age, parity, gravidity, and study site. Logistic regression analysis was used to calculate odds ratios (OR) and 95% confidence intervals (CI), adjusting for potential confounders. Statistical significance was set at $p < 0.05$. **Results:** A total of 148 EP (cases) and 296 IUP (controls) were analyzed. Independent risk factors for EP included a history of prior EP (aOR = 38.45, 95% CI: 3.52 - 5.05, $p < 0.001$), history of surgical treatment for EP (aOR = -37.0, 95% CI: 3.32 - 4.40, $p < 0.001$), 1 - 4 induced abortions (aOR = 2.36, 95% CI: 3.54 - 3.80, $p < 0.001$), natural contraception methods (aOR = 3.14,

95% CI: 2.26 - 8.47, $p = 0.02$), tobacco use (aOR = 3.15, 95% CI: 1.90 - 5.23, $p < 0.001$), and maternal age over 30 years (aOR = 1.73, 95% CI: 2.16 - 2.90, $p = 0.03$). **Conclusion:** This study confirms that established risk factors for EP, notably prior EP and its surgical treatment, are strongly associated with the condition in Douala. These findings emphasize the importance of targeted interventions, including detailed obstetric history assessment and tailored counseling, to mitigate EP risk in this population.

Keywords

Ectopic Pregnancy, Risk Factors, Douala, Cameroon, Sub-Saharan Africa

1. Introduction

Ectopic pregnancy (EP) refers to the implantation and development of a fertilized ovum outside the uterine cavity, most commonly in the fallopian tubes (ampullary, isthmus, or infundibulum), but it can also occur in the ovaries, cervix, or abdomen [1] [2]. EP represents a significant threat to maternal health, as it can lead to life-threatening complications. First-trimester bleeding, a common obstetric symptom, often necessitates the exclusion of EP, given its potential severity. The global incidence of EP is generally estimated at 1% - 2% of all pregnancies, although recent estimates suggest that it could be as high as 8% [2]-[4].

EP is a major contributor to maternal morbidity and mortality worldwide, with its incidence and associated case fatality rates increasing between 1990 and 2021 [5]. In Africa, where access to timely and quality healthcare is often limited, delayed diagnosis and management of EP lead to particularly severe consequences [6]. Studies across the continent, including those in Nigeria, Guinea, Ivory Coast, and Cameroon, have reported varying prevalence rates for EP and its risk factors [7]-[10], emphasizing the need for context-specific research in each region.

Established risk factors for EP, which have remained largely unchanged over the years, include a history of prior EP, pelvic inflammatory disease (PID)—particularly those caused by *Chlamydia trachomatis*—tubal surgeries, assisted reproductive technologies, and a history of induced abortions [11]-[15]. Other factors, such as smoking, advanced maternal age, and the use of certain contraceptive methods, are also implicated [12].

In Cameroon, despite advancements in healthcare, EP remains a significant public health challenge [6]. Previous studies have highlighted the association between PID, tubal surgery, and sexually transmitted infections (STIs) as key risk factors for EP in the region [6]-[8] [16]. However, a comprehensive understanding of the current risk profile in referral hospitals in Douala, Cameroon, was crucial to optimize patient care. This study, therefore, aimed to assess the risk factors for EP in two referral hospitals in Douala to inform targeted interventions and improve patient outcomes.

2. Methods

2.1. Study Design, Period, and Site

This retrospective case-control study was conducted over a 5-month period (February 1 to June 30, 2023), reviewing data from 10 years (January 1, 2013 to December 31, 2022). The study took place in the Obstetrics and Gynecology departments of two tertiary referral hospitals in Douala, Cameroon: Douala General Hospital (DGH) and Gyneco-Obstetrics and Pediatric Hospital of Douala (GO-PHD). Both hospitals provide comprehensive reproductive health services, including medical and surgical (laparotomy and laparoscopy) management of ectopic pregnancies, and are involved in medical training and research.

2.2. Sample Size Calculation

The minimum sample size was calculated using the Schlesselman formula, with a 1:2 case-to-control ratio. Based on a previous Cameroonian study reporting an odds ratio (OR) of 13.18 (95% CI: 6.19 - 27.42) for pelvic inflammatory disease as a risk factor for ectopic pregnancy, the calculated minimum sample size was 39 cases and 78 controls (total 117).

2.2.1. Inclusion and Exclusion Criteria

- Case Group: Complete medical records ($\geq 95\%$ data on selected variables) of patients hospitalized for ectopic pregnancy.
- Control Group: Complete medical records of patients with intrauterine pregnancies (IUP) followed at the same hospitals.

The following cases were excluded:

- Case Group: Incomplete medical records ($< 95\%$ data on selected variables).
- Control Group: History of ectopic pregnancy.

2.2.2. Matching Criteria

Cases and controls were matched by age group, gravidity, and study site (1:2 ratio).

2.3. Data Collection

Data were collected from birth registers, operative notes, and medical records, including demographic, gynecological, obstetrical, surgical, medical, and toxicological information.

2.4. Data Management and Analysis

Data were analyzed using EPI Info 3.5.4 and Microsoft Excel 2007. Odds ratios (OR) with 95% confidence intervals (CI) were calculated to assess associations between variables. Logistic regression was used to control for confounding variables. Chi-square and Fisher's exact tests were used as appropriate.

2.5. Ethical Considerations

Ethical approval was obtained from the Ethics Committee of Universite des Mon-

tagnes (No. 2023/267/Udm/PR/CIE). Patient confidentiality and safety were maintained throughout the study.

3. Results

Of the 155 patient files initially identified with ectopic pregnancies (EUPs), 7 were excluded due to incompleteness. Consequently, 148 patient files with EUPs were included in the case group. For the control group, 296 patient files with intrauterine pregnancies (IUPs) were selected.

3.1. Bivariate Analysis of Socio-Demographic Characteristics of the Two Groups

Table 1 below summarizes the comparison of socio-demographic factors between the cases and the controls. Women in the (31 - 35) and >40 age groups had the highest odds of having ectopic pregnancy, while those in the age group (26 - 30) had the lowest. Regarding profession, being a housewife carried the highest risk of having EP. Both tobacco and alcohol use were significantly associated with an increased risk of ectopic pregnancy.

Table 1. Socio-demographic factors and ectopic pregnancy (bivariate analysis).

Variables	Cases (n, %)	Controls (n, %)	OR (95% CI)	p-value
Age (years)				
[16 - 20]	4 (2.7)	8 (2.7)	1.00 (0.26 - 3.36)	0.610
[21 - 25]	20 (13.5)	58 (19.6)	0.64 (0.36 - 1.10)	0.070
[26 - 30]	41 (27.7)	126 (42.6)	0.52 (0.34 - 0.79)	0.000
[31 - 35]	50 (33.8)	65 (22.0)	1.81 (1.17 - 2.81)	0.010
[36 - 40]	21 (14.2)	34 (11.5)	1.27 (0.70 - 2.28)	0.250
>40	12 (8.1)	5 (1.7)	5.14 (1.80 - 16.43)	0.000
Profession				
Private sector	40 (27.0)	68 (23.0)	1.24 (0.79 - 1.95)	0.210
Informal sector	3 (2.0)	12 (4.1)	0.49 (0.11 - 1.66)	0.200
Trader	5 (3.4)	12 (4.1)	0.83 (0.26 - 2.35)	0.480
Student	34 (23.0)	83 (28.0)	0.77 (0.48 - 1.21)	0.150
Civil servant	18 (12.2)	58 (19.6)	0.57 (0.31 - 1.00)	0.030
University pers.	19 (12.8)	28 (9.5)	1.41 (0.75 - 2.62)	0.180
Housewife	29 (19.6)	35 (11.8)	1.82 (1.05 - 3.11)	0.020
Lifestyle				
Tobacco use	9 (6.1)	6 (2)	3.13 (1.08 - 9.59)	0.030
Alcohol use	64 (43.2)	54 (18.2)	3.41 (2.2 - 5.3)	0.000

3.2. Bivariate Analysis of Obstetrical and Gynecological Factors in the Two Groups

As shown in **Table 2**, women with a gravidity of four or more pregnancies have a significantly higher risk of ectopic pregnancy (EP) (OR = 6.00, $p = 0.040$). However, no significant association was found between parity and the risk of EP. In terms of abortions, a history of one to four voluntary abortions was significantly linked to an increased risk of EP (OR = 2.23, $p = 0.000$). A history of pelvic inflammatory disease (PID), particularly when associated with *Chlamydia trachomatis* infection, was also identified as a significant risk factor for EP (OR = 2.12, $p = 0.000$).

Table 2. Gynecological and obstetrical history and ectopic pregnancy.

Variable	Cases (n, %)	Controls (n, %)	OR (95% CI)	p-value
Gravidity				
<4	79 (53.4)	225 (76)	0.36 (0.24 - 0.55)	0.000
≥4	25 (10.8)	18 (4.1)	6.00 (2.39 - 15.97)	0.040
Parity				
<4	135 (91.2)	279 (94.3)	0.63 (0.30 - 1.30)	0.160
≥4	13 (8.8)	17 (5.7)	1.69 (0.77 - 41.63)	0.800
Abortion History				
Spontaneous (1 - 5)	18 (12.2)	41 (13.9)	0.86 (0.47 - 1.55)	0.370
Voluntary (1 - 4)	95 (64.2)	132 (44.6)	2.23 (1.48 - 3.35)	0.000
Voluntary (>4)	2 (1.4)	2 (0.7)	2.01 (0.21 - 19.47)	0.410
History of IVF	1 (0.7)	0 (0.0)	0.87 (0.50 - 4.76)	0.330
Gynecological Diseases				
Endometriosis	1 (0.7)	1 (0.3)	2.01 (0.05 - 78.51)	0.560
PID	57 (37.8)	66 (22.3)	2.12 (1.37 - 3.26)	0.000
PID/Chlamydia t.	48 (32.4)	56 (18.9)	2.06 (1.31 - 3.23)	0.000
Contraceptive Use				
MPA + Progestogen-only pills	29 (19.6)	38 (12.8)	2.45 (1.30 - 4.63)	0.006
IUD	10 (6.8)	4 (1.4)	5.29 (1.66 - 19.68)	0.000
Condom	72 (48.6)	183 (61.8)	0.59 (0.39 - 0.87)	0.010
Natural methods + Coitus interruptus	17 (11.5)	18 (6.1)	2.07 (0.96 - 4.47)	0.060
Number of Sexual Partners				
<5	36 (24.3)	117 (39.5)	0.49 (0.31 - 0.76)	0.000
5 - 8	85 (57.4)	142 (48.0)	1.46 (0.98 - 2.18)	0.060
≥9	26 (17.6)	35 (11.8)	1.59 (0.91 - 2.76)	0.110
Previous Ectopic Pregnancy	19 (12.8)	0 (0.0)	43.45 (7.78 - 914.74)	0.000
Infertility Treatment	6 (4.1)	4 (1.4)	1.47 (0.39 - 5.59)	0.560

Other risk factors included the use of Medroxyprogesterone Acetate (MPA) (OR = 3.33, $p = 0.030$), intrauterine devices (IUDs) (OR = 5.29, $p = 0.000$), natural contraceptive methods (OR = 2.30, $p = 0.050$), and a previous ectopic pregnancy (OR = 43.45, $p = 0.000$). On the other hand, condom use (OR = 0.59, $p = 0.010$) and practicing safe sexual behavior (defined as having fewer than five sexual partners) (OR = 0.49, $p = 0.000$) were found to have a protective effect against the occurrence of EP.

3.3. Bivariate Analysis of Past Surgical History in the Two Groups

The most significant finding in **Table 3** is the strong association between a previous surgery for ectopic pregnancy and the increased risk of future ectopic pregnancies (OR = 38.28, $p = 0.000$). Other surgical histories, including myomectomy, cystectomy, cesarean section, pelvic abscess drainage, and appendectomy, did not show a statistically significant association with the risk of EP.

Table 3. Comparison of surgical history between cases (ectopic pregnancy) and controls (intra-uterine pregnancy).

Surgical History	Cases (n, %)	Controls (n, %)	OR (95% CI)	p-value
Surgery for Ectopic Pregnancy	17 (11.5%)	1 (0.3%)	38.28 (6.78 - 810.48)	0.000
Myomectomy	2 (1.4%)	10 (3.4%)	0.39 (0.06 - 1.64)	0.180
Cystectomy	3 (2%)	8 (2.7%)	0.74 (0.16 - 2.77)	0.470
Cesarean Section	11 (7.4%)	18 (6.1%)	1.24 (0.55 - 2.69)	0.360
Pelvic Abscess Drainage	1 (0.7%)	1 (0.3%)	2.01 (0.05 - 78.51)	0.560
Appendectomy	3 (2%)	3 (1%)	2.02 (0.34 - 11.87)	0.320

3.4. Multivariate Analysis of Risks Increasing the Risk of EP

All factors that showed significant association with the occurrence of EP were included in the multivariate regression models to study the independence of their effects. **Table 4** presents the results of a multivariate logistic regression analysis that evaluates the adjusted odds ratios (aOR) for various factors associated with the risk of ectopic pregnancy (EP). Age > 30 years, past history of EUP, surgery for EUP, tobacco use, and number of voluntary abortions (1 - 4) all emerged as significant risk factors for ectopic pregnancy in this analysis. Natural methods of contraception also showed a significant association with an increased risk of EP. Alcohol consumption, cumulative number of sexual partners, and past history of PID were not significant in the final multivariate model, indicating that other factors may better explain the risk of EP.

4. Discussion

This case-control study aimed to identify significant risk factors associated with

ectopic pregnancy (EP) in Douala, Cameroon. Our multivariate analysis revealed several key findings related to demographic, reproductive, and lifestyle factors.

Table 4. Multivariate analysis of risk factors of Ectopic pregnancies.

Variable	aOR	95% CI	p-value
Age > 30 years	1.75	1.06 - 2.91	0.0302
Married	1.43	0.88 - 2.32	0.1492
Housewife	1.70	0.91 - 3.18	0.0978
Gravidity \geq 4	2.46	0.92 - 7.11	0.753
Past history of PID	1.45	0.86 - 2.45	0.1621
Past history of EUP	38.45	5.06 - 292.42	0.0004
Surgery for EUP	37.01	4.40 - 310.98	0.0009
Alcohol	1.67	0.47 - 5.95	0.4256
Tobacco	3.15	1.90 - 5.23	0.0000
Condom	1.27	0.79 - 2.05	0.3246
Natural Methods	3.15	1.17 - 8.48	0.0234
Cumulative sexual partners > 5	1.58	0.95 - 2.63	0.0758
Number of voluntary abortions (1 - 4)	2.36	1.47 - 3.80	0.0004

4.1. Socio-Demographic Factors

The average age of the population in the case group was (31.26 ± 5.81) years, with an age above 30 years being a significant risk factor for EP. This relatively young age has been observed in several studies conducted in low- and middle-income countries (LMICs) [8] [17] [18] and was also noted by Abdullah Karaer in Türkiye [19]. While few authors did not find a significant age difference between the EP and intra-uterine pregnancy groups, our findings underscore the importance of considering age-related physiological changes when providing reproductive health counseling.

4.2. Obstetrical and Gynaecological Factors

Induced abortions, especially repeated ones, were strong independent predictors of EP in our study. This could be attributed to restrictive abortion laws in the region, which often lead to unsafe abortions carried out by untrained individuals. These unsafe procedures can result in ascending infections, ultimately leading to salpingitis and narrowing the lumen of the fallopian tubes. This reduces the movement of the fertilized ovum towards the uterine cavity, contributing to the risk of EP [8]. Similar findings have been reported both in developed countries [5] [13] and LMICs [9] [18]-[21].

In line with previous scientific literature, our study identified the past history

of EP and past history of tubal surgery as key predictors of EP. Tubal damage and adhesions resulting from the surgical management of EP or tubal surgery are primary pathophysiological mechanisms leading to the occurrence of EP [22]. Studies from both high-income countries and African nations have consistently identified these factors as significant predictors of EP [23]-[25].

Furthermore, a past history of pelvic inflammatory disease (PID) was associated with the occurrence of EP, with the association being stronger when PID was caused by *Chlamydia trachomatis*, even though not statistically significant. The role of PID and sexually transmitted infections (STIs) in the development of EP has been well-documented globally [7] [13] [26] [27]. The high incidence of PID, combined with suboptimal treatment due to poverty in our setting, is a notable contributor to this condition. Tubal damage caused by PID reduces the peristaltic movement of the ovum and impedes sperm migration, which can explain this association.

The use of intrauterine devices (IUDs) was found to increase the risk of EP by 5.29 times. Other hormonal contraceptives, such as Medroxyprogesterone Acetate (MPA), were also identified as risk factors for EP but without. Although our findings differ from the results of Mindjah *et al.* in Cameroon [8] and Parashi *et al.* in India, who did not find a significant association between Depo-Provera use and EP risk [28], this discrepancy may be due to the possibility of early conception occurring immediately after discontinuation of MPA. This phenomenon has also been described for other contraceptive methods, such as the Levonorgestrel implant [29]. The association of natural contraception with increased EP risk remains controversial in the literature. While authors like Karaer *et al.* and Zhang *et al.* corroborate our findings, others like McQueen report no such link [30]. The potential explanation for this increased risk with natural methods of contraception is the higher likelihood of unintended pregnancies, which may result in ectopic pregnancies.

Other factors, such as the number of lifetime sexual partners, early onset of sexual intercourse, being single, and a past history of appendectomy—described by several authors—were not present in our study.

4.3. Lifestyle Factors

Tobacco smoking was identified as a predictor of EP in this study, whereas alcohol consumption showed no significant relationship. The link between cigarette smoking and EP due to the harmful effects of nicotine on the cilia of the fallopian tubes, and consequently on the occurrence of EP, has been well-established in European and American studies [16]. Our finding was somewhat surprising, as women in our study population typically claim abstinence from smoking. This may suggest the impact of passive smoking or the presence of nicotine in other substances consumed in the population's diet.

4.4. Study Limitations

This retrospective study may be subject to recall bias, particularly when gathering

reproductive and surgical history. Additionally, its regional scope and the relatively small sample size limit the ability to generalize the findings to the broader population of the nation or continent.

5. Conclusion

In summary, our study identified several risk factors associated with ectopic pregnancy, including advanced maternal age, induced abortions (especially repeated ones), past history of PID (particularly when caused by *Chlamydia trachomatis*), tubal surgery, and the use of certain contraceptive methods such as IUDs and MPA. Additionally, tobacco smoking emerged as a lifestyle factor that may contribute to the increased risk of EP. These findings emphasize the need for improved sexual and reproductive health education, more accessible and safe abortion services, and better management of sexually transmitted infections to reduce the burden of ectopic pregnancies in Douala, Cameroon.

Ethical Considerations

This study received ethical approval from the Institutional Review Board (IRB) of The Faculty of Health Sciences, Université des Montagnes, as well as administrative authorization from the management of DGH and DGHOPH. To protect patient confidentiality, all data were coded and anonymized. Verbal consent was obtained from patients who provided information regarding their post-surgery sexual life and self-perception.

Availability of Data and Materials

The datasets (patient medical files) are available at DGH and GOPHD upon reasonable request.

Authors' Contributions

RT, TNN, FMN, and CTN conceptualized and designed the study. MGT, FKM, and CJNN were responsible for recruiting participants at the study sites. AGSW and HNT also contributed to participant recruitment and provided feedback on the manuscript. The manuscript was written by TNN, RT, TOE, and FMN. HE, GHE, and CTN critically revised and reviewed the manuscript for important intellectual content. All authors read and approved the final version of the manuscript.

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Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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Appendix: Data Collection Sheet

Sheet Number: _____ Telephone Number: _____

Initials of the Patient's Name: _____

Case Control

A. Identification

1. Age: _____

2. Nationality: Cameroonian / _____

1 = Yes 2 = No If not, specify your origin: _____

3. Region of Origin: _____

1 = West 2 = Centre 3 = Littoral 4 = North
5 = North-West 6 = South-West 7 = South 8 = Far North
9 = Adamawa 10 = East

4. Marital Status: _____

1 = Single 2 = Married 3 = Widow 4 = Divorced
5 = Open relationship

5. Profession: _____

1 = Public sector 2 = Private sector 3 = Parapublic sector
4 = Trader 5 = Pupil 6 = Student
7 = Housewife

B. Past History

Obstetrical

6. Number of pregnancies: _____

Number of children delivered at term: _____

7. Number of induced abortions: _____

Number of spontaneous abortions: _____

8. Past history of ectopic pregnancy: _____

1 = Yes (If yes, specify number: _____)
2 = No

9. Fertility treatment history: _____

1 = Yes (Specify: Clomiphene citrate Others _____)
2 = No

10. *In vitro* fertilization (IVF) history: _____

1 = Yes 2 = No

Gynecological

11. Number of cumulative sexual partners: _____

12. Endometriosis history: _____

1 = Yes 2 = No

13. Tubal pathology history: _____

1 = Yes 2 = No

14. Contraceptive use history: _____

1 = Intrauterine contraceptive device (IUD) 2 = Progesterone-only pills

3 = Condoms 4 = Others (Specify: ____)

15. Pelvic inflammatory disease (PID) history: ____

1 = Chlamydia with IgG \geq 128 2 = Others (Specify: ____) 3 = No

Surgical

16. Surgical history: (Check all applicable)

- Surgery for ectopic pregnancy Myomectomy
- Cystectomy Cesarean section (If yes, number: _)
- Drainage of pelvic abscess Others (Specify: _)

Toxicology

17. Tobacco use: ____

1 = Yes (If yes, specify number of pack-years: ____) 2 = No

18. Alcohol consumption: ____

1 = Yes (Check one: Absolutely Occasionally Frequently)
2 = No

19. Other past history: ____

1 = Yes (If yes, specify: ____) 2 = No

C. Clinical Evaluation

20. Amenorrhea: ____

1 = Yes 2 = No

21. Pelvic pain: ____

1 = Yes 2 = No

22. Per vaginal bleeding: ____

1 = Yes 2 = No

23. Gestational age (in days): ____

1 = \leq 42 2 = 42 - 49 3 = \geq 49

D. Anatomic Location of the Ectopic Pregnancy

24. Tubal location: ____

1 = Yes (If yes, specify: Left Right Ampullary Isthmic Fimbrial
 Interstitial Unknown)

2 = No

25. Ovarian location: ____

1 = Yes 2 = No

26. Abdominal location: ____

1 = Yes 2 = No

27. Heterotopic location: ____

1 = Yes 2 = No

E. State of the Tubes and Associated Pathology

28. Ectopic pregnancy state: ____

1 = Ruptured 2 = Non-ruptured 3 = Fissurated

29. Homolateral tube state: ____

1 = Normal 2 = Abnormal 3 = Absent 4 = Unknown

30. Contralateral tube state: ____

1 = Normal 2 = Abnormal 3 = Absent 4 = Unknown

31. Associated pathologies: ____

1 = Hydrosalpinx 2 = Uterine fibroid 3 = Ovarian cyst

4 = Chlamydia cyst 5 = Adhesions 6 = None

F. Treatment of Ectopic Pregnancy

32. Medical treatment with methotrexate: ____

1 = Yes 2 = No

33. Route of methotrexate administration: ____

1 = Parenteral 2 = Local

34. Methotrexate protocol: ____

1 = Single dose 2 = Multi-dose

35. Adjuvant treatment with folate: _

1 = Yes 2 = No

36. Surgical treatment: ____

1 = Yes 2 = No

37. Surgical route: ____

1 = Laparotomy 2 = Laparoscopy

38. Radical surgical management: ____

1 = Yes 2 = No

39. If yes, specify: ____

1 = Total salpingectomy 2 = Adnexectomy 3 = Unknown

40. Conservative surgical treatment: ____

1 = Yes 2 = No

41. If yes, specify: ____

1 = Partial salpingectomy

2 = Tubal expression

3 = Salpingotomy

4 = Partial oophorectomy

5 = Partial salpingectomy plus end-to-end anastomosis

6 = Unknown