Original Research

# IDENTIFICATION OF KEY RISK FACTORS FOR ECTOPIC PREGNANCY: A CASE-CONTROL STUDY AMONG PAKISTANI WOMEN

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## ABSTRACT

**Objective**: To determine and examine the most important risk factors that lead to ectopic pregnancies in Pakistani women in terms of reproductive history, contraceptive use, and surgical history.

**Place and Duration**: The study was performed at Karachi Metropolitan University Abbasi Shaheed Hospital Karachi during March 2025 to March 2026.

**Methods**: In this study, 250 pregnant women were recruited as controls, and 125 women with ectopic pregnancy. Ectopic pregnancy diagnosis was established using detailed menstrual history, physical examination, serial β-human chorionic gonadotropin (βhCG) testing, and abdominal/transvaginal ultrasonography. A questionnaire was used to collect demographic, menstrual, and reproductive information. The statistical analysis was conducted with SPSS version 16, and binary logistic regression was used to calculate odds ratios (OR) and 95% confidence intervals (CI).

**Results**: The study found significant associations between ectopic pregnancy and abdominal/pelvic surgery (OR=5.09, 95% CI 1.95-12.81, p<0.001), IUD use (OR=4.54, 95% CI 1.53-13.12, p<0.001), and tubal ligation (OR=4.22, 95% CI 1.09-16.34, p<0.001). Ectopic pregnancy history was highly predictive (OR=60.72, 95% CI 6.45-510.22, p<0.001). Other factors, such as abortion (OR=6.12, 95% CI 3.67-10.39) and age, exhibited weaker relationships with p-values of 0.92 and 0.08, respectively.

**Conclusion**: Women with a prior history of ectopic pregnancy, abdominal/pelvic surgery, IUD, and tubal ligation were at a significant risk of ectopic pregnancy. These observations underscore the importance of pre-conception counseling and early screening programs to alleviate maternal morbidity. More research is necessary to determine the importance of infections and other possible risk factors in ectopic pregnancy.

**Keywords**: Ectopic Pregnancy, Risk Factors, Abdominal Surgery, Pakistan.

## INTRODUCTION

Ectopic pregnancy (EP) refers to the implantation of a fertilized ovum outside the uterine cavity, mostly in the fallopian tube, and is still identified as one of the most severe early pregnancy complications in obstetric practice [1]. It contributes to about 1-2% of total reported pregnancies and a disproportionate burden of first-trimester pregnancy losses and complications [2]. The etiology of ectopic

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pregnancy is multifactorial in nature, yet it is essentially caused by a disruption in normal tubal transportation and a change in reproductive tract microenvironments that delays or blocks embryo migration into the uterine cavity [3]. Recent studies in reproductive biology emphasize that, in addition to classical anatomic interference, intricate interactions among local inflammation, immunologic changes, microbial factors and hormonal influences may predispose to ectopic implantation [4].

A cornerstone of EP epidemiology is the identification of risk factors that change tubal integrity or host susceptibility. One of the most regularly reported risk factors globally has historically been pelvic inflammatory disease (PID), in most cases, caused by sexually transmitted infections, since it impairs the ciliary function and the structural arrangement of the fallopian tubes, thereby obstructing the passage of the embryo [2, 5]. Among the most replicated risk exposures are infectious and inflammatory sequelae. PID, particularly cervical infections caused by chlamydia and gonorrhea that extend to affect the fallopian tubes, has been attributed to causing tubal damage and consequently ectopic implantation [5]. Although low-grade, subclinical inflammation may lead to epithelial disruption and ciliary dysfunction, significantly increasing ectopic risk in women with such inflammation [6].

In South and Southeast Asian studies, past ectopic pregnancy, prior pelvic or abdominal surgical operation (including cesarean section), intrauterine device (IUD) at conception, and smoking have been found to be important predictors [7]. PID and miscarriage have been reported in Pakistan as the most prevalent risk profiles in some hospital series [8]. There is consistent evidence that PID is the most prevalent attributable cause (prevalence to 87.5% in recent cohorts), followed by previous miscarriage or induced abortion (72.5%), infertility, and pelvic surgeries, which is increased by endemic genital tuberculosis, limited STI screening, and sociocultural barriers to early antenatal care [9].

Although there have been improvements in diagnostic imaging and minimally invasive surgical procedures, management of ectopic pregnancies is still not optimal in most healthcare facilities in Pakistan [10]. Limited reproductive health education and inadequate access to family planning services are key factors in the effective management of EP [11]. In order to overcome the issues faced by ectopic pregnancies, Pakistan requires a comprehensive solution to address the problem through early detection, management plans and education of the population through awareness creation about reproductive health among women. This study aims to determine and examine the major risk factors that cause ectopic pregnancies in Pakistani women.

## METHODOLOGY

This was a hospital-based case-control study in which 250 pregnant women were used as controls and 125 women diagnosed with ectopic pregnancy were used in this case. In the case group, ectopic pregnancy was diagnosed by a combination of detailed menstrual history, comprehensive physical examination, serial quantitative β-human chorionic gonadotropin (βhCG) assays, and confirmatory abdominal or transvaginal ultrasonography. In all cases, a history of delayed or missed menstruation followed by nonspecific early symptoms such as lower abdominal pain or tenderness, which is either dull or sharp and diffuse or localized, with irregular spotting or vaginal bleeding. Cervical motion tenderness and abdominal tenderness were frequently noted in clinical examination.

Data on the control group were gathered from pregnant women who had no complications, and their questionnaire did not include any diagnostic procedures like 1gCG or ultrasound. Data from both groups were based on hospital medical records. Two control-group women were selected to be matched with each case-patient woman. The case-patient group data collection involved a questionnaire that included details on demographic characteristics, menstrual history, pregnancy status, diagnostic steps, and management. Conversely, the questionnaire administered to the control group omitted the diagnostic actions and management section.

The SPSS version 16 (SPSS Inc., Chicago, IL, USA) was used to conduct statistical analysis. To determine the relationship between ectopic pregnancy and potential risk factors, binary logistic regression was applied to obtain odds ratios (OR) and 95% confidence intervals (CI). The multivariate model incorporated the variables identified as significant in the univariate analysis to test associations even in the presence of confounders.

## RESULTS

A total of 250 women in the control group and 125 women in the case group diagnosed with ectopic pregnancy. Among the control group, the majority of women were aged 21-25 (n=80, 32.0%) and had no history of abortion (n=215, 86.0%). In contrast, the case group showed a higher proportion of women aged 26-30 (n=50, 40.0%) and with a history of abortion (n=48, 38.4%). The odds of abortion in the case group were significantly higher (OR=6.12, 95% CI 3.67-10.39). Parity distribution was similar across both groups, with no significant differences in educational levels (Table 1).

Table 1: Distribution of Age, Educational Level, Parity, and History of Abortion among Ectopic Pregnancy Cases and Matched Controls

| Variable | Control (N=250) | Case (N=125) | Crude OR | 95% CI |
|---|---|---|---|---|
| **Age (Y)** | | | | |
| 15-20 | 40 (16.0%) | 7 (5.6%) | 0.32 | 0.14-0.74 |
| 21-25 | 80 (32.0%) | 30 (24.0%) | 0.72 | 0.43-1.18 |
| 26-30 | 65 (26.0%) | 50 (40.0%) | 1.54 | 1.00-2.38 |
| 31-35 | 50 (20.0%) | 31 (24.8%) | 1.22 | 0.76-1.96 |
| 36+ | 15 (6.0%) | 7 (5.6%) | 1 | - |
| **Educational Level** | | | | |
| 0-8 | 145 (58.0%) | 66 (52.8%) | 0.88 | 0.30-2.61 |
| 9-12 | 65 (26.0%) | 40 (32.0%) | 1.33 | 0.48-3.73 |
| 13-18 | 15 (6.0%) | 8 (6.4%) | 1 | - |
| Missing | 25 (10.0%) | 11 (8.8%) | - | - |
| **Parity** | | | | |
| 0 | 125 (50.0%) | 45 (36.0%) | 1.15 | 0.56-2.38 |
| 1 | 75 (30.0%) | 47 (37.6%) | 1.25 | 0.68-2.34 |
| 2+ | 50 (20.0%) | 33 (26.4%) | 1 | - |
| **Abortion** | | | | |
| 0 | 215 (86.0%) | 56 (44.8%) | 0.13 | 0.07-0.21 |
| 1 | 20 (8.0%) | 48 (38.4%) | 6.12 | 3.67-10.39 |
| 2+ | 15 (6.0%) | 21 (16.8%) | 1 | - |

The case group (n=125, 33.3%) had significantly higher outcomes for abdominal/pelvic surgery (OR=5.09, 95% CI 1.95-12.81, p<0.001), IUD use (OR=4.54, 95% CI 1.53-13.12, p<0.001), and tubal ligation (TL) (OR=4.22, 95% CI 1.09-16.34, p<0.001) compared to the control group (n=250, 66.7%). Ectopic pregnancy history showed a very high association (OR=60.72, 95% CI 6.45-510.22, p<0.001) with increased odds in the case group. Other factors like abortion and age showed less significant associations, with p-values of 0.92 and 0.08, respectively (Table 2).

Table 2: Adjusted Risk Factors Associated With Ectopic Pregnancy after Final Logistic Regression Analysis

| Variable | Adjusted OR | 95% CI | P Value |
|---|---|---|---|
| Age (Y) | 2.12 | 0.79-5.67 | 0.08 |
| Abortion | 1.02 | 0.33-2.98 | 0.92 |
| Ectopic pregnancy | 60.72 | 6.45-510.22 | <0.001 |
| Abdominal/Pelvic surgery | 5.09 | 1.95-12.81 | <0.001 |
| IUD | 4.54 | 1.53-13.12 | <0.001 |
| TL | 4.22 | 1.09-16.34 | <0.001 |
| Tubal surgery | 0.38 | 0.04-3.41 | 0.43 |
| Tubal pathology | 0.31 | 0.01-7.72 | 0.48 |
| ART | 1.75 | 0.13-19.71 | 0.64 |
| Infertility | 1.68 | 0.36-8.44 | 0.49 |
| Oral contraception | 0.65 | 0.21-2.06 | 0.50 |

*IUD: Intrauterine device; TL: Tubal ligation; ART: Assisted reproductive technology*

The case group showed significantly higher use of IUD (n=34, 27.2%) compared to the control group (n=12, 4.8%) with an OR of 6.01 (95% CI: 3.10-11.60). Tubal ligation (TL) was more common in the case group (n=12, 9.6%) than the control group (n=5, 2.0%), with an OR of 5.40 (95% CI: 1.80-14.90). The case group also had significantly higher rates of ectopic pregnancy (n=33, 26.4%) compared to the control group (n=1, 0.4%) with an OR of 84.00 (95% CI: 11.40-623.70). Abdominal/pelvic surgery showed a marked difference, with the case group having higher instances (n=49, 39.2%) compared to the control group (n=8, 3.2%), yielding an OR of 17.80 (95% CI: 8.10-38.70). Factors like infertility and tubal pathology showed less pronounced associations (Table 3).

Table 3: Contraceptive Method Use and Associated Risk in Ectopic Pregnancy Cases versus Controls

| Variable | Control (N=250) | Case (N=125) | Crude OR | 95% CI |
|---|---|---|---|---|
| Contraceptive Methods | | | | |

| | | | | |
|---|---|---|---|---|
| IUD | Yes (n=12, 4.8%) | Yes (n=34, 27.2%) | 6.01 | 3.10-11.60 |
| | No (n=238, 95.2%) | No (n=91, 72.8%) | | |
| Oral Contraception | Yes (n=24, 8.0%) | Yes (n=8, 6.4%) | 0.60 | 0.28-1.50 |
| | No (n=276, 92.0%) | No (n=117, 93.6%) | | |
| TL | Yes (n=5, 2.0%) | Yes (n=12, 9.6%) | 5.40 | 1.80-14.90 |
| | No (n=245, 98.0%) | No (n=113, 90.4%) | | |
| High Risk Factors | | | | |
| Ectopic Pregnancy | No (n=249, 99.6%) | Yes (n=33, 26.4%) | 84.00 | 11.40-623.70 |
| | Yes (n=1, 0.4%) | No (n=92, 73.6%) | | |
| Tubal Pathology | No (n=247, 98.8%) | Yes (n=3, 2.4%) | 2.10 | 0.40-10.10 |
| | Yes (n=3, 1.2%) | No (n=122, 97.6%) | | |
| Tubal Surgery | No (n=245, 98.0%) | Yes (n=5, 4.0%) | 2.58 | 0.67-9.60 |
| | Yes (n=5, 2.0%) | No (n=120, 96.0%) | | |
| Moderate Risk Factors | | | | |
| Infertility | No (n=243, 97.2%) | Yes (n=14, 11.2%) | 1.70 | 0.40-7.00 |
| | Yes (n=7, 2.8%) | No (n=111, 88.8%) | | |
| Low Risk Factors | | | | |
| Abdominal/Pelvic Surgery | No (n=242, 96.8%) | Yes (n=49, 39.2%) | 17.80 | 8.10-38.70 |
| | Yes (n=8, 3.2%) | No (n=76, 60.8%) | | |

## DISCUSSION

The present study assessed the primary risk factors linked to ectopic pregnancy through a comparison of women diagnosed with ectopic pregnancies (cases) and pregnant controls who did not have ectopic pregnancy. We found strong relationships with surgical history, contraceptive use, and prior ectopic pregnancy. Ectopic pregnancy history has a high odds ratio (OR = 60.72) in our analysis, and women who have had another ectopic pregnancy are much more likely to get one. This is consistent with a study conducted by Kaplan et al., which showed an increased recurrence rate 5-10 times higher in women with a history of ectopic pregnancies than in women without such a history [12].

Our study also showed a strong association between abdominal/pelvic surgery and ectopic pregnancy (OR = 5.09). Past pelvic or abdominal surgeries may lead to adhesions and alterations in normal tubal anatomy, thereby increasing the risk of abnormal implantation. In one study, Harish et al. found that prior pelvic/abdominal surgery was also a major factor in the incidence of EP [13]. Our result of heightened risk with IUD is consistent with Suliman et al., who also mentioned IUD use and prior pelvic or tubal surgery to be the most prevalent risk factors, though with a lesser occurrence rate than ours (IUD 3.6% and TL 2.4% in that study compared to 27.2% and 9.6% in our cases) [14]. Conversely, Biggs et al. have noted that in some groups, very low sensitivity in detecting EP has been observed with simple screening criteria such as IUD history, suggesting that IUD history alone is not a useful predictive measure in isolation [15].

Tubal ligation also proved to be a key factor in the current study. Studies on the results of tubal ligation indicate that post-sterilization EP is rare, but when fertility recurs, it is more likely to be ectopic because of the interference with tubal architecture [16]. Conversely, other factors had weaker or non-significant associations. For example, infertility, ART, and oral contraceptive use were not significant effects of our adjusted model. This is contrary to Moustakli et al., in which ART, especially in vitro fertilization, has been reported to contribute to ectopic risk because of the changed embryo transfer dynamics and underlying tubal pathology [17]. The findings of Papageorgiou et al. validated that previous EP, tubal pathology and ART are the primary predictors of ectopic implantation, reinforcing the biological process of disrupted embryo transport [18].

Interestingly, our adjusted model indicated less significant or no significant relationships between abortion history and maternal age. This is in comparison to the Mahajan et al. case-control study, in which induced abortion and infertility were reported to raise EP risk and age >30 to have higher EP incidence, presumably because of cumulative reproductive exposures [19]. Similarly, Njamen et al. found advanced maternal age and induced abortions as independent risk factors in addition to PID and the use of IUDs [20]. Such disparities are probably due to demographic and behavioral differences; perhaps in some populations, abortion activity or age distributions may affect tubal integrity and hormonal milieu more than in others.

The fact that we found that IUD users were significantly more likely to have ectopic pregnancy than non-users is consistent with the findings of Jahanfar et al., who found that IUD users who become pregnant had significantly higher odds of ectopic than intrauterine pregnancy (pooled OR ≈ 4.38) [21]. We also found that the odds of ectopic pregnancy were very high in the case of prior ectopic gestations (OR = 84.00). This is well

supported by the results of Aich et al., which repeatedly discover that recurrence risk is one of the most credible predictors of a subsequent ectopic pregnancy [22].

The implications of the findings are significant to clinical practice and public health. First, they support the necessity of specific pre-conception education about the risks of IUD and tubal ligation failures, especially in women with any previous pelvic surgery or history of ectopic pregnancies. Second, routine early ultrasound screening for at-risk women would be integrated to reduce rupture rates in similar regional cohorts. Lastly, reinforcing STI prevention and post-procedure follow-up interventions in Pakistan and similar low- and middle-income nations could resolve the upstream infectious and surgical morbidities contributing to these high-risk odds.

The study is limited by its hospital-based design, which may not fully represent the general population of women in Pakistan, as it excludes women without access to healthcare. Also, some of the variables used in the study rely on medical records and self-report data, which may introduce reporting bias or inaccuracies.

## CONCLUSION

In this study, some of the major risk factors of ectopic pregnancy among Pakistani women were identified, and these included women with a history of ectopic pregnancy, abdominal/pelvic surgeries, IUD, and tubal ligation. Future studies, including prospective cohort studies, are required to confirm these results, determine the role of infections in ectopic pregnancy and the efficacy of early screening measures to minimize maternal morbidity. Such insights would guide community-based health programs and enhance the handling of ectopic pregnancies in Pakistan and other countries.

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