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Predictors and clinical characteristics of ruptured ectopic pregnancy: A retrospective analysis

Rüptüre ektopik gebeliğin risk faktörleri ve klinik özellikleri: Retrospektif bir inceleme

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ABSTRACT

Aim: This study aimed to identify and analyze the specific risk factors and clinical characteristics associated with tubal rupture in women with ectopic pregnancy (EP).

Materials and Methods: A retrospective analysis was conducted on 180 women diagnosed with EP at a tertiary care center between 2015 and 2024. Patients were stratified into two groups: those with tubal rupture (n=132) and those with unruptured EP (n=48). Patient demographics, reproductive history, presenting clinical signs, serum beta-human chorionic gonadotropin (β-hCG) levels, and operative outcomes were collected.

Results: Women with ruptured EP were significantly younger (31.2 ± 5.5 vs. 33.3 ± 5.8 years; $p = 0.026$) and presented with significantly lower mean serum β-hCG concentrations (3037.9 ± 4438.5 vs. 5483.6 ± 5300.8 mIU/mL; $p = 0.006$). A history of a prior EP and tubal surgery was more frequent among unruptured cases ($p = 0.018$ and $p = 0.017$, respectively). In multivariable logistic regression, younger age (adjusted odds ratio [aOR] 0.91; 95% CI, 0.84–0.98; $p = 0.018$), the presence of abdominal pain (aOR 3.27; 95% CI, 1.06–10.05; $p = 0.039$), and lower serum β-hCG ($p < 0.001$) were confirmed as independent predictors of rupture. Salpingectomy was the predominant surgical procedure in ruptured cases (97.7%) compared to unruptured cases (89.6%; $p = 0.006$).

Conclusion: Tubal rupture in EP was independently associated with younger age, lower serum β-hCG levels, and the presence of abdominal pain. A history of EP was observed more frequently among unruptured cases.

Keywords: Ectopic pregnancy, β-hCG, abdominal pain, salpingectomy

ÖZ

Amaç: *Bu çalışmanın amacı, ektopik gebeliği (EG) olan kadınlarda tubal rüptür ile ilişkili özgül risk faktörlerini ve klinik özellikleri belirlemek ve analiz etmektir.*

Gereç ve Yöntem: *2015–2024 yılları arasında üçüncü basamak bir sağlık merkezinde EG tanısı alan 180 kadın retrospektif olarak incelendi.*

Hastalar iki gruba ayrıldı: tubal rüptür gelişenler (n=132) ve rüptür gelişmeyen EG olguları (n=48). Hastaların demografik özellikleri, üreme öyküleri, başvuru sırasındaki klinik bulguları, serum beta-human chorionic gonadotropin (β-hCG) düzeyleri ve cerrahi sonuçları değerlendirildi.

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Bulgular: *Rüptüre EG olguları anlamlı olarak daha genç (31,2 ± 5,5 vs. 33,3 ± 5,8 yıl; p=0,026) ve ortalama serum β-hCG düzeyleri daha düşüktü (3037,9 ± 4438,5 vs. 5483,6 ± 5300,8 mIU/mL; p=0,006). Önceki EG öyküsü ve tubal cerrahi öyküsü, rüptür gelişmeyen olgularda daha sık saptandı (sırasıyla p=0,018 ve p=0,017). Çok değişkenli lojistik regresyon analizinde; daha genç yaş (düzeltilmiş olasılık oranı [aOR] 0,91; %95 GA, 0,84–0,98; p=0,018), karın ağrısı varlığı (aOR 3,27; %95 GA, 1,06–10,05; p=0,039) ve düşük serum β-hCG düzeyleri (p<0,001) bağımsız rüptür öngördürücüleri olarak doğrulandı. Cerrahi tedavide salpenjektomi, rüptüre olgularda baskın prosedür olarak uygulandı (%97,7), bu oran rüptür gelişmeyenlerde daha düşüktü (%89,6; p=0,006).*

Sonuç: *Ektopik gebelikte tubal rüptür, bağımsız olarak daha genç yaş, düşük serum β-hCG düzeyleri ve karın ağrısı varlığı ile ilişkili bulundu. Önceki ektopik gebelik öyküsü ise rüptür gelişmeyen olgularda daha sık gözlendi.*

Anahtar Sözcükler: *Ektopik gebelik, β-hCG, karın ağrısı, salpenjektomi*

INTRODUCTION

Ectopic pregnancy (EP), defined as implantation of a fertilized ovum outside the uterine cavity, is a major gynecological emergency and the leading cause of first-trimester maternal mortality. Globally, EP accounts for an estimated 5–10% of pregnancy-related deaths and up to 75% of first-trimester maternal mortality (1). Although advances in transvaginal ultrasonography (TVUS) and serial measurement of serum β-human chorionic gonadotropin (β-hCG) have reduced mortality in developed countries, EP remains a substantial health burden, particularly in resource-limited settings. Its incidence appears to be rising, a trend attributed to increasing rates of pelvic inflammatory disease (PID), greater use of assisted reproductive technologies (ART), and higher cesarean section prevalence (2).

The most catastrophic complication of EP is tubal rupture, which can precipitate massive intra-abdominal hemorrhage, hemodynamic collapse, and death. Diagnosis is often challenging because many patients present with nonspecific or atypical symptoms. The classic triad of abdominal pain, vaginal bleeding, and amenorrhea occurs in fewer than half of cases and overlaps with other conditions such as miscarriage, appendicitis, and ovarian cyst rupture, leading to frequent delays in recognition (3).

Current diagnostic standards, clinical evaluation, TVUS, and serial β-hCG are highly effective for identifying EP but have limited predictive value for rupture. Importantly, rupture has been reported at both very low and very high β-hCG levels, undermining the assumption that higher concentrations necessarily reflect greater risk (4,5). Similarly, the role of maternal age in rupture risk remains uncertain (6,7). To address these gaps, this retrospective study was undertaken to identify independent predictors of tubal rupture and to compare the clinical and perioperative characteristics of ruptured versus unruptured ectopic pregnancies.

MATERIALS and METHODS

Study Design and Ethical Considerations

This was a single-center, retrospective observational study of patients diagnosed with EP who were admitted to Kartal City Hospital between January 2015 and January 2024. The study protocol was reviewed and approved by the Research Ethics Committee of the Hospital (number: 2024/14/891). The study was conducted in accordance with the ethical principles outlined in the Declaration of Helsinki. The requirement for informed written consent was waived by the institutional review board as it involved the analysis of anonymized, non-identifiable patient data and presented no direct risk to the subjects.

Patient Population and Data Collection

Inclusion criteria for the study were women who were admitted with a diagnosis of EP and underwent surgical intervention. Patients were identified and data were abstracted from the hospital's electronic medical record system.

Exclusion criteria included women with confirmed intrauterine pregnancies, those who received medical treatment with methotrexate, and those for whom surgical intervention was not indicated. Additionally, patients whose medical records were incomplete or lacked data, were excluded from the final analysis.

Clinical Variables and Outcomes

A comprehensive set of clinical and demographic variables was abstracted from the medical

records. These included patient age, initial clinical presentation (e.g., abdominal pain, vaginal bleeding), admission serum β-human chorionic gonadotropin (β-hCG) levels, the location of the EP, and operative details. Operative data included the treatment route (laparoscopy or laparotomy), the surgical method (salpingectomy or salpingostomy), operation time, and estimated blood loss. The requirement for blood transfusion and the duration of the hospital stay were also recorded.

Patients were then stratified into two groups based on the operative finding of the EP: ruptured or unruptured. A ruptured EP was defined as an operative finding of significant hemoperitoneum and/or tubal wall defect or avulsion necessitating urgent surgical intervention (8). The primary outcome of the study was the occurrence of tubal rupture. Secondary outcomes included the surgical route, surgical method, operation time, pre- and postoperative hemoglobin levels, duration of hospital stay, and transfusion requirement.

Statistical Analysis

Continuous variables were assessed for normality using the Shapiro–Wilk test. Normally distributed data are presented as mean (standard deviation), while non-normally distributed data are presented as median (interquartile range). Categorical variables are presented as counts and percentages. Comparisons between the ruptured and unruptured groups were performed using the Student's t-test or the Mann–Whitney U test for continuous variables and the chi-squared ($\chi 2$) test or Fisher's exact test for categorical variables, as appropriate.

Univariable logistic regression analyses were conducted to estimate crude odds ratios (ORs) and 95% confidence intervals (CIs) for potential risk factors associated with tubal rupture. Variables with a p-value < 0.10 in the univariable analysis and those considered clinically relevant *a priori* were included in a multivariable logistic regression model to estimate adjusted odds ratios (aORs) and 95% CIs. The final model was assessed for multicollinearity using Variance Inflation Factors (VIFs), with a VIF < 5 considered acceptable to ensure the stability of the model's coefficients. The overall model calibration was assessed using the Hosmer–Lemeshow goodness-of-fit test, where a non-significant p-value (p > 0.05) indicated an adequate fit between observed and predicted outcomes. A two-sided p-value < 0.05 was considered statistically significant for all primary and secondary outcome analyses. All statistical analyses were performed using R statistical software, version 4.3.2.

RESULTS

Patient Characteristics

A total of 180 women with EP were included, of whom 132 (73.3%) presented with tubal rupture and 48 (26.7%) had unruptured ectopic pregnancies. Women with rupture were significantly younger than those with unruptured cases (31.2 ± 5.5 vs 33.3 ± 5.8 years, $p = 0.026$). Mean serum β-hCG concentration was lower among ruptured cases (3037.9 ± 4438.5 vs 5483.6 ± 5300.8 mIU/mL, $p = 0.006$), with a significantly higher proportion in the 100–999 mIU/mL category ($p = 0.005$). Gestational age, parity, history of abdominal surgery, abdominal pain at presentation, and vaginal bleeding were not significantly different between groups. A history of EP and prior tubal surgery were more frequent among unruptured cases ($p = 0.018$ and $p = 0.017$, respectively). (Table-1)

Operative and Postoperative Findings

Laparoscopy was more frequently performed in ruptured cases compared with unruptured cases (78.8% vs 64.6%), but the difference did not reach statistical significance (p = 0.079). Salpingectomy was the predominant procedure overall and was performed more often in ruptured cases (97.7% vs 89.6%; p = 0.006). The laterality of the affected tube and the small number of ovarian EP were similar between groups. Mean operative time, transfusion rates, postoperative hemoglobin, and length of hospital stay were comparable between groups (all p > 0.05) (Table-2).

Factors Associated with Rupture

In univariable analysis, younger age, lower serum β-hCG, and absence of prior tubal surgery or EP were associated with rupture. Multivariable logistic regression confirmed younger age (adjusted OR [aOR] 0.91; 95% CI, 0.84–0.98; $p = 0.018$), presence of abdominal pain (aOR 3.27; 95% CI, 1.06–10.05; $p = 0.039$), and lower serum β-hCG ($p < 0.001$) as independent predictors of rupture (Table-3). Vaginal bleeding demonstrated a borderline inverse association (aOR 0.45; $p = 0.065$). Surgical method correlated with rupture status, with salpingostomy associated with lower odds compared with salpingectomy (aOR 0.03;

95% CI, 0.00–0.29; $p = 0.003$), though this likely reflects treatment selection rather than a causal relationship. Other perioperative variables, including surgical route, operative time, transfusion requirement, postoperative hemoglobin, and hospital stay, were not independently associated with rupture.

Table-1. Baseline Characteristics of Study Participants

Variable	Unruptured (n=48)	Ruptured (n=132)	p value
Age (years)	33.3 ± 5.8	31.2 ± 5.5	0.026
Gestational age (weeks)	4.9 ± 1.6	4.9 ± 1.7	0.989
Parity	1.3 ± 1.0	1.2 ± 1.0	0.383
Serum β-hCG (mIU/mL)	5483.6 ± 5300.8	3037.9 ± 4438.5	0.006
Preoperative Hb (mg/dL)	11.9 ± 1.4	11.5 ± 1.7	0.077
β-hCG categories (mIU/mL)			0.005
<100	1 (2.1%)	2 (1.5%)	
100–999	5 (10.4%)	50 (37.9%)	
1000–9999	38 (79.2%)	75 (56.8%)	
≥10000	4 (8.3%)	5 (3.8%)	
History of ectopic pregnancy			0.018
Yes	9 (18.8%)	8 (6.1%)	
No	39 (81.2%)	124 (93.9%)	
History of abdominal surgery			1.000
Yes	25 (52.1%)	68 (51.5%)	
No	23 (47.9%)	64 (48.5%)	
History of tubal surgery			0.017
Yes	7 (14.6%)	5 (3.8%)	
No	41 (85.4%)	127 (96.2%)	
Abdominal pain			0.316
Yes	8 (16.7%)	33 (25.0%)	
No	40 (83.3%)	99 (75.0%)	
Vaginal bleeding			0.237
Yes	26 (54.2%)	57 (43.2%)	
No	22 (45.8%)	75 (56.8%)	

A p value of <0.05 indicates a significant difference.

Table-2. Operative and Postoperative Characteristics

Variable	Unruptured (n=48)	Ruptured (n=132)	p value
Surgical route			0.079
Laparoscopy	31 (64.6%)	104 (78.8%)	
Laparotomy	17 (35.4%)	28 (21.2%)	
Surgical method			0.006
Salpingectomy	43 (89.6%)	129 (97.7%)	
Salpingostomy	5 (10.4%)	1 (0.8%)	
Location			0.389
Right tube	23 (47.9%)	74 (56.1%)	
Left tube	25 (52.1%)	56 (42.4%)	
Left ovary	0 (0.0%)	2 (1.5%)	
Operation time (min)	44.8 ± 19.1	44.8 ± 14.4	0.985
Transfusion			0.397
Yes	7 (14.6%)	28 (21.2%)	
No	41 (85.4%)	104 (78.8%)	
Postoperative Hb (mg/dL)	10.8 ± 1.1	10.4 ± 1.3	0.062
Length of hospital stay (days)	3.3 ± 1.1	3.1 ± 1.3	0.480

A p value of <0.05 indicates a significant difference.

Table-3. Univariable and Multivariable Analyses of Factors Associated with Tubal Rupture

Variable	Crude OR (95% CI)	p value	Adjusted OR (95% CI)	p value
Age (year)	0.93 (0.88–0.99)	0.024	0.91 (0.84–0.98)	0.018
Gestational age (weeks)	1.00 (0.82–1.22)	0.989	1.08 (0.84–1.39)	0.560
Parity	0.87 (0.63–1.19)	0.386	1.00 (0.64–1.58)	0.987
History of abdominal surgery	0.98 (0.50–1.89)	0.946	1.32 (0.55–3.14)	0.538
History of tubal surgery	0.23 (0.07–0.77)	0.017	0.53 (0.09–3.01)	0.473
Abdominal pain	1.67 (0.71–3.92)	0.242	3.27 (1.06–10.05)	0.039
Vaginal bleeding	0.64 (0.33–1.25)	0.193	0.45 (0.19–1.05)	0.065
Serum β-hCG	1.00 (1.00–1.00)	0.009	1.00 (1.00–1.00)	<0.001
β-hCG category	0.36 (0.19–0.70)	0.002	—	—
History of ectopic pregnancy	0.28 (0.10–0.77)	0.014	0.35 (0.08–1.51)	0.157
Surgical route (laparotomy vs laparoscopy)	0.49 (0.24–1.01)	0.054	0.45 (0.18–1.13)	0.091
Surgical method (salpingostomy vs salpingectomy)	0.07 (0.01–0.59)	0.015	0.03 (0.00–0.29)	0.003
Operation time (min)	1.00 (0.98–1.02)	0.983	1.00 (0.98–1.03)	0.845
Postoperative hemoglobin (mg/dL)	0.78 (0.60–1.03)	0.082	0.71 (0.44–1.13)	0.146
Transfusion	1.55 (0.63–3.84)	0.340	0.57 (0.15–2.11)	0.400
Length of hospital stay (days)	0.92 (0.72–1.18)	0.515	0.84 (0.62–1.15)	0.283

A p value of <0.05 indicates a significant difference.

DISCUSSION

This retrospective observational study of 180 women with EP revealed a high prevalence of tubal rupture, which occurred in 73.3% of cases. This high rupture rate is consistent with a hospital-based population, which is often biased toward more severe presentations.[13] Multivariable analysis identified three independent predictors of rupture: younger maternal age, lower serum β-hCG levels, and the presence of abdominal pain. In addition, a history of EP and tubal surgery were more frequent in the unruptured group, reflecting the impact of heightened clinical surveillance in high-risk patients. Furthermore, salpingectomy was performed significantly more often in ruptured cases

The association between younger age and rupture contrasts with prior work linking advanced maternal age with overall EP risk. This finding may be attributable to the fact that women within this age group are at the peak of reproductive and sexual activity. Furthermore, young women are inherently more susceptible to sexually transmitted infections due to the persistence of columnar epithelium extending from the endocervical to the ectocervical canal, which increases mucosal exposure to pathogens including *Chlamydia trachomatis*, *Neisseria gonorrhoeae*, *Mycoplasma* spp., as well as mixed aerobic and anaerobic microorganisms (6,9). One possible explanation also is that older women, often with infertility or ART histories, are monitored more closely, facilitating earlier diagnosis and intervention.

Previous research have indicated that serum β-hCG levels exceeding 1750 mIU/mL are associated with a higher likelihood of ruptured EP (3). Similarly, another study reported that β-hCG levels above 5000 mIU/mL correlate with an increased risk of rupture (10). However, serum β-hCG levels are not reliable predictors of tubal EP rupture, as no threshold value has been identified that safely distinguishes ruptured from unruptured cases (5). Indeed, our study demonstrated that lower serum β-hCG levels were independently associated with an increased risk of rupture.

Abdominal pain is commonly observed in cases of tubal rupture and may present as unilateral, diffuse, or localized discomfort, often associated with hemoperitoneum (11). However, these symptoms are not specific to EP. Our multivariable analyses indicated a significant association between abdominal pain and ruptured EP, in agreement with previous studies (12). These results suggest that abdominal pain may serve as an important clinical indicator for assessing the risk of rupture in patients with suspected EP.

Ruptured EP constitutes a surgical emergency. Most case series report a lower proportion of ruptured cases compared with unruptured ectopic pregnancies. In a study by Darkhaneh et al., ruptured ectopic pregnancies represented 20.2%

of all EP cases (3), whereas another investigation reported a substantially higher proportion (59%) (10, 13). More recently, ruptured ectopic pregnancies have been documented to comprise up to 79% of cases (12). In the present study, ruptured ectopic pregnancies accounted for 73.3% of all EP cases.

A notable finding of the present study was that a history of EP was more frequently observed among patients with unruptured EP. Although several studies have reported a higher incidence of rupture in individuals with a history of EP (10, 14), other investigations have demonstrated a lower proportion of rupture within this subgroup (15). These inconsistent results highlight the need for further research to elucidate the relationship between prior EP and the risk of rupture.

This study has several limitations. Its retrospective design limits causal inference, and recruitment from a single center may introduce selection bias, warranting confirmation in multicenter or population-based studies. The small sample size reduces statistical power and generalizability. In addition, lack of detailed ultrasound parameters, including tubal diameter, implantation site, hemoperitoneum volume, stricts deeper pathophysiologic interpretation.

CONCLUSION

This study demonstrates that younger age, lower serum β-hCG, and abdominal pain are independent predictors of tubal rupture in EP. The higher prevalence of a history of previous EP and tubal surgery among unruptured cases suggests that heightened clinical awareness in high-risk groups may lead to earlier diagnosis and prevention of rupture.

Conflicts of interest: Authors declared no conflict of interest

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