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REVIEW ARTICLE

Prevalence and Related Factors of Rupture among Cases with Ectopic Pregnancy; a Systematic Review and Meta-Analysis

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Abstract: **Introduction:** In the absence of timely treatment, the risk of rupture in patients with ectopic pregnancy (EP) increases, which is associated with extensive bleeding, complicated surgery, and maternal death. This study aimed to investigate the prevalence of rupture and its related factors among EP cases. **Methods:** A comprehensive, systematic search was conducted in electronic databases, such as Scopus, PubMed, Web of Science, and Persian electronic databases such as Iranmedex, and Scientific Information Database using keywords extracted from Medical Subject Headings such as "Ectopic pregnancies", "Extrauterine pregnancies", and "Ruptured ectopic pregnancy" from the earliest to the 13th of December 2022. The CMA program, version 3, was utilized for analysis. The overall effect size was calculated using the sample size and the frequency of rupture in each of the studies. Heterogeneity was measured using the I2 statistics. **Results:** A total of 5,269 women with EP participated in 17 studies. The pooled prevalence of rupture was 56.4% (95%CI: 44.9% to 67.2%; I2=98.09%; P<0.001). Factors such as number of parties, amount of -hCG, age, history of ectopic pregnancy, cornual and isthmic pregnancies, gestational age, number of gravidities, history of tubal ligation, tubal diameters, periods of infertility, history of infertility, pregnancy by ovulation induction, extensive hemoperitoneum, ampullar and isthmic pregnancies, ampullar pregnancies, preoperative heart rate (HR), triage, triage shock index (SI), abdominal pain, single marital status, preoperative hemoglobin levels, preoperative hematocrit levels, history of pelvic inflammatory disease (PID), and use of contraceptives were associated with the prevalence of rupture in EP cases. **Conclusion:** Based on the findings, 56.4% of EP cases experienced rupture and various factors influence its prevalence. As a result, health managers and policymakers can address and mitigate modifiable factors contributing to rupture in EP cases by implementing regular consultations and screenings.

Keywords: Ectopic pregnancies; Extrauterine pregnancies; Ruptured ectopic pregnancy; Meta-analysis

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1. Introduction

Ectopic pregnancy (EP) is a potentially life-threatening gynecology condition to maternal life in the first trimester (1). The term “EP” is used to describe the implantation of a developing blastocyst outside the uterine endometrium (2). Broadly, EP is divided into tubal, non-tubal, and heterotopic pregnancy types, which refers to the simultaneous presence of intrauterine and extrauterine pregnancy (3). In the majority of

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EP cases, the implantation site is the fallopian tube. However, it can occur in the cervix, ovary, abdomen, previous cesarean scar, the rudimentary horn of a uni-cornuate uterus, and the interstitial part of the tube (4). Estimates worldwide suggest that 1-2% of all pregnancies may be EPs (5). Various factors are known to be associated with the occurrence of EP, including fallopian tube damage, pelvic inflammatory disease, previous tubal surgery, previous EP, and history of assisted reproductive technologies (6).

Women with EP are involved with a wide range of clinical manifestations from asymptomatic cases to severe abdominal pain and hemodynamic shock, which is why EP has become a challenge for obstetricians and gynecologists (7).

Even though EP is the cause of 10-15% of maternal deaths (8). Early diagnosis and choosing the optimal treatment approach can make the person survive and reduce side effects (9). The diagnosis of EP is made with a combination of clinical and laboratory examinations, and ultrasound is the best method of symptomatic affirmation (10). However, the absence of fetal heart sounds outside the uterine cavity does not always mean the absence of EP, and laparoscopy or laparotomy may be used for the final diagnosis (11). Considering the circumstances, treatment options can range from medication administration to laparotomy (12).

In the absence of timely treatment, the risk of rupture in women with EP increases as the gestational age increases, which is associated with consequences such as extensive bleeding, the need for blood transfusions, complicated surgery, and maternal death (13). The manifestations of rupture may be acute, with severe acute abdominal discomfort, shock, and hemoperitoneum, or subacute with abdominal pain, amenorrhea, and vaginal bleeding (11).

Few previous research has focused on determining the factors affecting the occurrence of REP (14-16). However, limited studies have identified the ability of different factors to predict the risk of rupture in EPs. This systematic review and meta-analysis aimed to investigate the prevalence and related factors of rupture among EP cases.

2. Methods

This systematic review and meta-analysis was carried out utilizing the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) checklist (17). Additionally, the current review was not listed in the database of the International Prospective Register of Systematic Reviews (PROSPERO).

2.1. Patient/population, Exposure, and outcomes (PEO) framework

The PEO framework was used to clarify the purpose of the study. Accordingly, population (EP acses), exposure (rupture), and outcome (prevalece and related factors), were included in the systematic review and meta-analysis (Table 1).

2.2. Search strategy

A comprehensive, systematic search was conducted in different international electronic databases, such as Scopus, PubMed, Web of Science, and Persian electronic databases such as Iranmedex, and Scientific Information Database (SID) using keywords extracted from Medical Subject Headings (MeSH) such as ((“Women with ectopic pregnancy”) OR (“Pregnant women”) OR (“Pregnancy”)) AND ((“Ectopic pregnancies”) OR (“Extrauterine pregnancies”) OR (“Ruptured ectopic pregnancies”) OR (“Unruptured ectopic pregnancies”)) AND ((“Prevalence”) OR (“Incidence”) OR (“Epidemiology”) OR (“Frequency”) OR (“Burden”)) from the earliest to December 13, 2022. For example, the search strategy was in PubMed/MEDLINE database including ((“Women with ectopic pregnancy”) OR (“Pregnant women”) OR (“Pregnancy”)) AND ((“Ectopic pregnancies”) OR (“Extrauterine pregnancies”) OR (“Ruptured ectopic pregnancies”) OR (“Unruptured ectopic pregnancies”)) AND ((“Prevalence”) OR (“Incidence”) OR (“Epidemiology”) OR (“Frequency”) OR (“Burden”)). The search strategy is presented in Table 2. The Boolean operators "OR" and "AND" were utilized to join terms. Iranian electronic databases’ Persian keyword equivalents were also looked up. Separately, two researchers conducted a thorough search. This systematic review and meta-analysis exclude gray literature, which includes expert commentary, conference presentations, theses, research and committee reports, and ongoing research. Gray literature is written in print or electronically, but it hasn’t been given the publisher’s seal of approval for commercial publication (18).

2.3. Inclusion and exclusion criteria

This systematic review and meta-analysis looked at cross-sectional research on the prevalence of rupture in women with EP and its contributing factors that were written in Persian and English and published in both languages. Research with qualitative designs, reviews, case reports, conference proceedings, letters to the editor, and experiments were excluded.

2.4. Study selection

The data management program utilized for this systematic review and meta-analysis is EndNote X8. Two researchers independently reviewed the study titles and abstracts, the full text of the publications, and the removal of duplicate studies both electronically and manually based on the inclusion and exclusion criteria. The third researcher resolved any disagreements between the first two researchers while selecting the studies. Finally, references were carefully examined to prevent data loss.

2.5. Data extraction and quality assessment

The information extracted in this review by the researchers includes the name of the first author, year of publication, location, sample size, age, gestational age, gravidity, parity, abortion, unruptured EP (UEP)/REP, and the key result. The appraisal tool for cross-sectional studies (AXIS tool) evaluates the quality of the included studies via 20 items with a two-point Likert, including yes (score of 1) and no (score of 0). This tool assesses report quality (7 items), study design quality (7 items), and the possible introduction of biases (6 items). Finally, AXIS rates the quality of studies at three levels: high (70 to 100%), fair (60 to 69.9%), and low (0 to 59.9%) (19).

2.6. Statistical analysis

The CMA program, version 3, was utilized for analysis. The overall effect size was calculated using the sample size and the frequency of REP in each of the studies. Heterogeneity was measured using the I2 statistics. Mild, moderate, and high heterogeneity are defined, respectively, as I2 values of 25%, 50%, and 75%. Due to the considerable level of result variability, the random effects model had to be used.

2.7. Sensitivity analysis

To determine how each study's absence would impact the prevalence of REP overall, a sensitivity analysis was carried out.

2.8. Publication of bias

The Egger test results and a Funnel plot were used to assess the publishing of bias.

3. Results

3.1. Study Selection

As shown in Figure 1, a comprehensive search of electronic databases yielded 2,029 studies. Due to duplicate articles, 390 articles were excluded from the study. Out of the 1,639 articles that were left, 104 studies were omitted from the systematic review and meta-analysis because they were not cross-sectional, and 1,492 publications were excluded because they did not correspond with the study's objectives. Following a thorough analysis of the papers' full texts, eight research were discarded for having insufficient data, and fourteen studies were disqualified due to poor design or findings. In conclusion, this systematic review and meta-analysis included seventeen studies (3, 11, 20-34).

3.2. Study Characteristics

As mentioned in Table 3, a total of 5,269 women with EP participated in 17 studies (3, 11, 20-34). Their mean age was 28.86 years (SD=5.34). Studies were conducted in the USA (n=3) (24, 26, 31), Turkey (n=2) (28, 30), Iran (n=2) (25, 27), Pakistan (n=2) (11, 22), Canada (n=) (33), France (n=1) (29), Lithuania (n=1) (23), Greece (n=1) (34), Sudan (n=1) (20), India (n=1) (21), Taiwan (n=1) (32), and Ghana (n=1) (3).

3.3. Quality of included study

As shown in Table 4, all of the studies (3, 11, 20-34) were of high quality. In addition, eleven studies (11, 20-24, 27-31) failed to disclose funding sources or potential conflicts of interest, while ten (11, 21, 23, 25, 26, 28-31, 33) failed to disclose research limitations.

3.4. Prevalence of rupture

As shown in Figure 2, the pooled prevalence of rupture in women with EP was 56.4% (95%CI: 44.9% to 67.2%; I2=98.09%; P<0.001).

3.5. Sensitivity analysis

As seen in Figure 3, sensitivity analyses were performed to see how each study's removal influenced the overall results and between-study heterogeneity.

3.6. Publication bias

As shown in Figure 4, the Egger regression test supported the publishing bias that was evident in the symmetric funnel plot for the prevalence of REP (t=2.34, P=0.03).

3.7. Associated Factors of rupture

As shown in table 3, number of parity (n=8) (11, 20, 22, 23, 27, 32-34), amount of -hCG (n=5) (21, 25, 28, 29, 31), amount of fluid recorded on ultrasonography (n=3) (21, 26, 30), age (n=2) (25, 27), history of EP (n=2) (31, 34), cornual and isthmic pregnancies (n=2) (23, 29), gestational age (n=1) (28), number of gravidity (n=1) (27), history of tubal ligation (n=1) (27), tubal diameters (n=1) (33), periods of infertility (n=1) (29), history of infertility (n=1) (29), pregnancy by ovulation induction (n=1) (29), extensive hemoperitoneum (n=1) (29), ampullar and isthmic pregnancies (n=1) (21), ampullar pregnancies (n=1) (3), preoperative heart rate (HR) (n=1) (30), triage HR (n=1) (24), triage shock index (SI) (n=1) (24), abdominal pain (n=1) (32), and single marital status (n=1) (3) were among the factors which had a higher rate in ruptured EPs in comparison to unruptured EPs.

Also, factors such as preoperative hemoglobin levels (n=5) (24, 26, 30, 32, 33), gestational age (n=2) (25, 32), history of infertility (n=2) (20, 27), age (n=1) (22), preoperative hematocrit levels (n=1) (30), history of pelvic inflammatory disease (PID) (n=1) (23), use of contraceptives (n=1) (29), and history of EP (n=1) (33) had a lower rate in the ruptured EPs than in the unruptured group.

4. Discussion

The systematic review and meta-analysis, which incorporated seventeen cross-sectional studies involving 5,269 women diagnosed with EP, revealed that 56.4% of these women experienced rupture. Factors associated with rupture in women with EP included the number of parties, amount of -hCG, age, history of EP, cornual and isthmic pregnancies, gestational age, number of gravidities, history of tubal ligation, tubal diameters, periods of infertility, history of infertility, pregnancy by ovulation induction, extensive hemoperitoneum, ampullar and isthmic pregnancies, ampullar pregnancies, preoperative HR, triage HR, triage SI, abdominal pain, single marital status, preoperative hemoglobin levels, preoperative hematocrit levels, history of PID, and use of contraceptives.

The medical disorder known as an EP occurs when the fertilized ovum implants itself somewhere other than the normal uterine cavity (35). In individuals experiencing rupture, the gestational sac within the fallopian tube undergoes expansion beyond the tube's capacity. Detecting rupture at an early stage is of utmost significance (36).

In this current systematic review and meta-analysis, it was determined that 56.4% of women with EP experienced rupture. The findings from a systematic review and meta-analysis conducted on the occurrence of EP among expectant mothers in Ethiopia revealed that the primary course of action for these patients was salpingectomy, primarily due to the high prevalence of rupture (37).

The results of this study showed that one of the influencing factors on REP is age. The study of Faraji et al. in Iran showed that with increasing age, the possibility of REP prevalence increases (27). Nonetheless, a study conducted in Pakistan revealed that younger pregnant mothers have a higher likelihood of experiencing rupture (22). Based on the findings from the systematic review and meta-analysis, further research is warranted to comprehensively investigate the impact of age on the occurrence of rupture. The existing articles exhibit heterogeneity in their results, highlighting the need for additional studies to establish a more precise understanding of this relationship.

An influential aspect explored in the research examined within this systematic review and meta-analysis concerning the elevated occurrence of rupture in mothers with ectopic pregnancies was the number of children a woman had previously given birth to, which is often referred to as parity (11, 20, 22, 23, 27, 32-34). The relationship between a greater number of previous parity and an elevated risk of REP can be elucidated by several factors, including the formation of scar tissue and adhesions, as well as an increased likelihood of tubal damage. In women who have experienced multiple pregnancies and childbirths, there is an increased propensity for the development of scar tissue and adhesions within their fallopian tubes and pelvic area (38). This scar tissue can create obstacles for the fertilized egg's passage through the fallopian tube to the uterus, consequently elevating the risk of entrapment and the subsequent occurrence of a rupture. With each pregnancy and childbirth, there is the potential for increased stress and damage to the fallopian tubes, rendering them more susceptible to injury or obstructions (39). This, in turn, can hinder the typical movement of the fertilized egg and elevate the risk of EP.

The findings derived from the studies encompassed in this systematic review and meta-analysis indicate that mothers with EPs who exhibited lower preoperative hemoglobin levels were more likely to experience rupture (24, 26, 30, 32, 33). Reduced preoperative hemoglobin levels can signify anemia or diminished oxygen-carrying capacity in the bloodstream, potentially compromising the ability to sustain a developing EP (40). Consequently, this condition elevates the likelihood of the rupture, resulting in more severe complications. It is crucial to emphasize that, although this correlation is present, various other factors can impact the risk of a ruptured EP, underscoring the importance of a thorough clinical evaluation for accurate diagnosis and effective management.

Another factor that influenced the prevalence of rupture was the history of EP. In this systematic review and meta-analysis, two studies reported a higher incidence of rupture among individuals with a previous history of EP (31, 34). However, a different study yielded contrary results, indicating a lower percentage of rupture occurrence in patients with a history of EP (33). Considering these conflicting results, it is suggested that future studies investigate the relationship between EP history and rupture.

Another influencing factor on the prevalence of rupture in this study was the history of infertility. In this systematic review and meta-analysis, the studies included presented conflicting findings concerning the relationship between infertility history and the prevalence of REP. While two studies indicated a lower prevalence of rupture in individuals with a history of infertility (20, 27), another study suggested a direct association between infertility history and rupture occurrence (29). Based on the findings obtained, there is a need for further investigation into the potential relationship between the history of infertility in women and the occurrence of rupture.

The study's results demonstrated that the urine beta hCG levels in subjects with rupture were higher compared to those with unrupture EPs (21, 25, 28, 29, 31). This suggests that beta hCG levels can serve as a diagnostic factor in identifying cases of rupture.

Rupture is a serious clinical disorder that can lead to disability and death in people. According to the results of the present study, many factors influence the prevalence of rupture in EP cases. Therefore, health managers and policy-

makers can reduce and eliminate modifiable factors affecting rupture by scheduling consultations and periodic screenings of EP cases.

It is suggested that more studies be conducted about the related and predictive factors of rupture in EPs. Additionally, it is recommended that investigations look into what causes the association between related factors and rupture. It is also suggested that according to the obtained results and the factors related to the prevalence of rupture, experimental studies should be conducted to investigate effective interventions and pieces of training on reducing the amount of rupture in EPs.

5. Limitations

This systematic review and meta-analysis only include research that was written in English and Persian; studies that were written in other languages were likely overlooked.

6. Conclusion

In sum, in this systematic review and meta-analysis, it was found that 56.4% of women with EP experienced rupture. Also, the findings showed that various factors influence the prevalence of rupture in them. As a result, health managers and policymakers can address and mitigate modifiable factors contributing to rupture by implementing regular consultations and screenings for women with EP.

7. Declarations

7.1. Acknowledgments

None.

7.2. Conflict of interest

The authors declare no conflict of interest.

7.3. Funding and support

None.

7.4. Authors' contribution

Study concept and design by all authors; Data acquisition by all authors; Data interpretation by all authors; drafting of the manuscript by all authors; Revision of the manuscript by all authors; the final version of the manuscript is approved by all authors.

7.5. Data availability

The datasets generated and analyzed during the current study are available from the corresponding author upon reasonable request.

7.6. Using artificial intelligence chatbots

The authors declare that they have not used artificial intelligence chatbots.

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and Therapeutic Medicine. 2018;16(6):4712-6.

Table 1: PEO framework and search strategy terms

PEO	Keywords	#*	Search Terms
Population	Women with ectopic pregnancy	1	((“Women with ectopic pregnancy”) OR ((“Ectopic pregnancies”) OR (“Extrauterine pregnancies”))
Exposure	Rupture	2	((“Ruptured ectopic pregnancies”) OR (“Unruptured ectopic pregnancies”))
Outcome	Prevalence and related factor	3	((“Prevalence”) OR (“Incidence”) OR (“Epidemiology”) OR (“Frequency”) OR (“Burden”))

* #1, #2, and #3 combined with “AND” operator. √ To widen search results and avoid missing data, terms for comparison and outcomes were not included in the search strategy.

Table 2: Search strategy

Databases	Search strategy
Scopus	((“ectopic pregnancy”) OR (“Ectopic pregnancies”) OR (“Extrauterine pregnancies”)) AND (“Ruptured ectopic pregnancies”) OR (“Unruptured ectopic pregnancies”)) AND ((“Prevalence”) OR (“Incidence”) OR (“Epidemiology”) OR (“Frequency”) OR (“Burden”))
PubMed	((“ectopic pregnancy”) OR (“Pregnant women”) OR (“Pregnancy”)) AND ((“Ectopic pregnancies”) OR (“Extrauterine pregnancies”) OR (“Ruptured ectopic pregnancies”) OR (“Unruptured ectopic pregnancies”)) AND ((“Prevalence”) OR (“Incidence”) OR (“Epidemiology”) OR (“Frequency”) OR (“Burden”))
WOS	((“ectopic pregnancy”) OR (“Pregnant women”) OR (“Pregnancy”)) AND ((“Ectopic pregnancies”) OR (“Extrauterine pregnancies”) OR (“Ruptured ectopic pregnancies”) OR (“Unruptured ectopic pregnancies”)) AND ((“Prevalence”) OR (“Incidence”) OR (“Epidemiology”) OR (“Frequency”) OR (“Burden”))

WOS: Web of Science

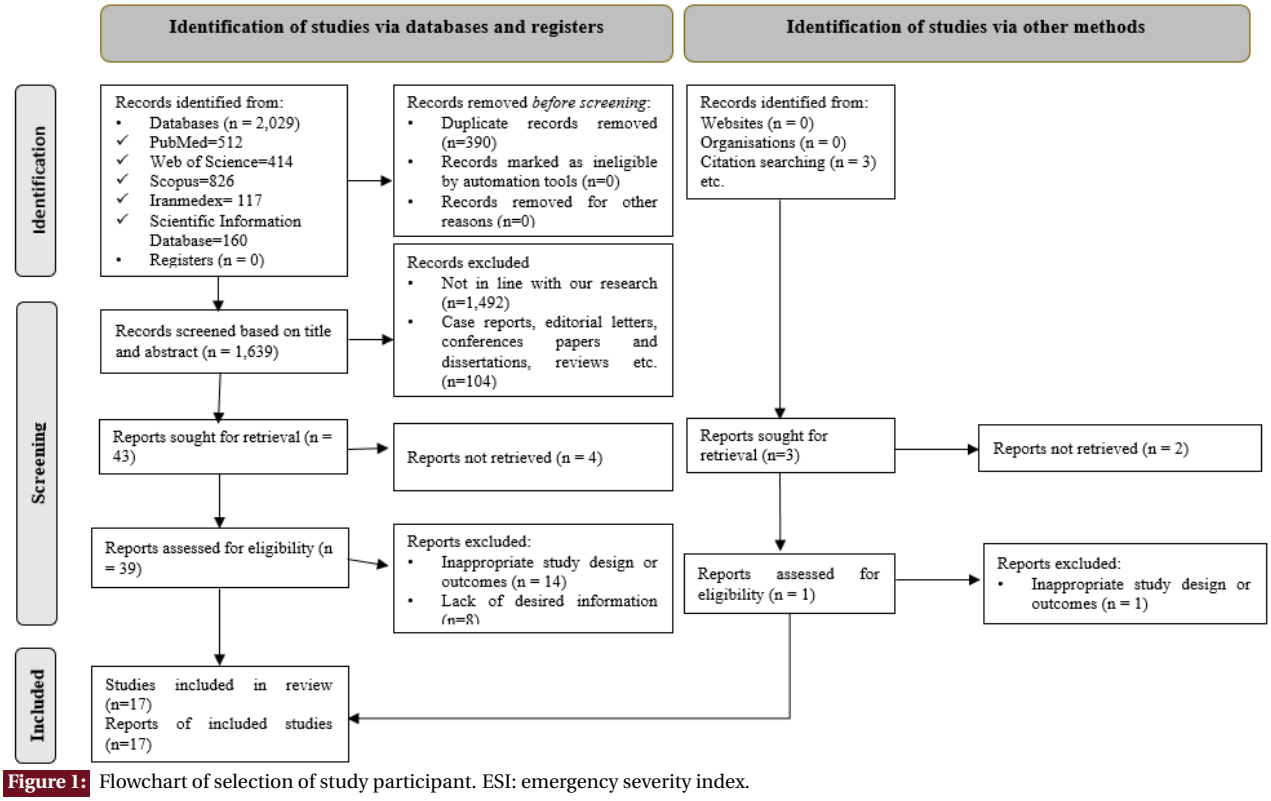

Figure 1: Flowchart of selection of study participant. ESI: emergency severity index.

Table 3: Basic characteristics of the included studies in this systematic review and meta-analysis

First Author year	Location	Sample size	Age (year)	Gestational age (weeks)	Gravidity	Parity	Abortion	UEP/ REP (%)	Key results	AXIS Score
Saxon et al., 1997 (33)	Canada	693	• UEP: 30.30 (SD = 5.10) • REP: 30.80 (SD = 5.80) • Total: 30.55 (SD = 5.45)	• UEP: 6.90 (SD = 1.90) • REP: 7.20 (SD = 2.20)	• UEP: 2.80 (SD = 1.70) • REP: 3.00 (SD = 2.00)	• UEP: 0.80 (SD = 1.00) • REP: 1.00 (SD = 1.30)	• UEP: 1.00 (SD = 1.20) • REP: 1.00 (SD = 1.50)	66.23/ 33.77	• Patients in the REP group had a higher number of parity than the UEP group (P=0.002). • Patients in the REP group had lower preoperative hemoglobin levels than the UEP group (P<0.001). • Patients in the REP group had higher tubal diameters before surgery than the UEP group (P=0.012). • Patients in the REP group had a history of EP lower than the UEP group (P=0.04).	High
Falcone et al., 1998 (26)	USA	236	• UEP: 30.50 (SD = 5.10) • REP: 30.70 (SD = 4.90) • Total: 30.60 (SD = 5.00)	• UEP: 7.30 (SD = 1.90) • REP: 6.90 (SD = 1.90)	• UEP: 2.70 (SD = 1.40) • REP: 3.00 (SD = 1.50)	• UEP: 0.70 (SD = 0.90) • REP: 0.90 (SD = 1.20)	• UEP: 1.00 (SD = 1.20) • REP: 1.10 (SD = 1.20)	73.73/ 26.27	• Patients in the REP group had lower preoperative hemoglobin levels than the UEP group (P<0.001). • There was a significant positive relationship between the amount of fluid recorded on ultrasonography and the frequency of REP (P<0.001).	High
Job-Spira et al., 1999 (29)	France	849	N/A	N/A	N/A	N/A	N/A	81.98/ 18.02	• Patients in the REP group had periods of infertility of at least 1 year more than the UEP group (P<0.01). • Patients in the REP group had a history of infertility associated with prior tubal damage more than the UEP group (P<0.01). • Patients in the REP group had a lower proportion of used contraception than the UEP group (P<0.01). • Patients in the REP group had more than the UEP group (P<0.01). • Patients in the REP group had a higher amount of -hCG than the UEP group (P<0.001). • Patients in the REP group had extensive hemoperitoneum more than the UEP group (P<0.001). • There was a greater risk of REP for cornual and isthmic pregnancies than other sites of ectopic pregnancies (P<0.01).	High
Brikhahn et al., 2003 (24)	USA	52	• UEP: 31.00 (SD = N/A) • REP: 31.00 (SD = N/A) • Total: 31.00 (SD = N/A)	• UEP: 6.57 (SD = N/A) • REP: 6.42 (SD = N/A)	N/A	N/A	N/A	51.93/ 48.07	• Patients in the REP group had a higher Triage HR than the UEP group (P<0.0001). • Patients in the REP group had a higher Triage SI than the UEP group (P<0.0001). • Patients in the REP group had lower preoperative hemoglobin levels than the UEP group (P=0.01).	High

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First Author year	Location	Sample size	Age (year)	Gestational age (weeks)	Gravidity	Parity	Abortion	UEP/ REP (%)	Key results	AXIS Score
Latchaw et al., 2005 (31)	USA	738	• UEP: 29.20 (SD = 6.00) • REP: 29.70 (SD = 6.40) • Total: 29.45 (SD = 6.20)	N/A	N/A	N/A	N/A	40.51/ 59.49	• Patients in the REP group had a history of EP more than the UEP group (P<0.001). • Patients in the REP group had a higher amount of -hCG than the UEP group (P<0.001).	High
Berlingieri et al., 2007 (23)	Lithuania	879	N/A	N/A	N/A	N/A	N/A	70.53/ 29.47	• Patients in the REP group had a higher number of parity than the UEP group (P=0.006). • Patients in the REP group had a history of PID lower than the UEP group (P=0.023). • There was a greater risk of REP for cornual and isthmic pregnancies than other sites of ectopic pregnancies (P<0.001). • There was a significant positive relationship between and REP (P<0.001).	High
Sindos et al., 2009 (34)	Greece	223	• UEP: 29.10 (SD = 5.10) • REP: 30.20 (SD = 4.70) • Total: 29.65 (SD = 4.90)	• UEP: 7.55 (SD = N/A) • REP: 7.70 (SD = N/A)	N/A	• UEP: 0.85 (SD = 0.89) • REP: 1.19 (SD = 1.02)	N/A	35.43/ 64.57	• Patients in the REP group had a higher number of parity than the UEP group (P=0.015). • Patients in the REP group had a history of EP more than the UEP group (P<0.019).	High
Ali et al., 2011 (20)	Sudan	199	• UEP: 30.30 (SD = 6.70) • REP: 27.80 (SD = 6.30) • Total: 27.90 (SD = 6.30)	N/A	N/A	• UEP: 2.80 (SD = 2.30) • REP: 5.10 (SD = 2.60)	N/A	6.53/ 93.47	• Patients in the REP group had a higher number of parity than the UEP group (P=0.003). • Patients in the REP group had a history of infertility lower than the UEP group (P<0.01). • Patients in the REP group had a lower level of education than the UEP group (P<0.01).	High
Goksedef et al., 2011 (28)	Turkey	232	• UEP: 28.90 (SD = 5.60) • REP: 29.60 (SD = 5.60) • Total: 29.16 (SD = 5.60)	• UEP: 6.40 (SD = 1.20) • REP: 7.80 (SD = 1.09)	N/A	N/A	N/A	62.07/ 37.93	• Patients in the REP group had higher gestational age than the UEP group (P<0.0001). • Patients in the REP group had a higher amount of -hCG than the UEP group (P<0.0001).	High
Faraji et al., 2013 (27)	Iran	180	• UEP: N/A • REP: N/A • Total: 24.94 (SD = N/A)	• UEP: 7.36 (SD = 1.78) • REP: 7.38 (SD = 1.50)	• UEP: 2.00 (SD = 1.37) • REP: 2.53 (SD = 1.44)	• UEP: 0.06 (SD = 1.10) • REP: 1.06 (SD = 1.19)	• UEP: 1.34 (SD = 0.72) • REP: 0.43 (SD = 0.77)	55.55/ 44.45	• Patients in the REP group had a higher number of gravidity than the UEP group (P=0.01). • Patients in the REP group had a higher number of parity than the UEP group (P=0.007). • Patients in the REP group had a history of infertility lower than the UEP group (P=0.005). • Patients in the REP group had a history of tubal ligation more than the UEP group (P=0.01). • There was a significant positive relationship between age and REP (P=0.001).	High

Table 3: Basic characteristics of the included studies in this systematic review and meta-analysis

First Author year	Location	Sample size	Age (year)	Gestational age (weeks)	Gravidity	Parity	Abortion	UEP/ REP (%)	Key results	AXIS Score
Kaya et al., 2013 (30)	Tukey	188	• UEP: 32.07 (SD = 5.66) • REP: 31.69 (SD = 6.31) • Total: 31.80 (SD = 5.98)	N/A	• UEP: 2.61 (SD = 2.31) • REP: 2.75 (SD = 2.04)	• UEP: 1.54 (SD = 1.24) • REP: 1.62 (SD = 1.64)	N/A	30.32/ 68.68	• Patients in the REP group had lower preoperative hemoglobin levels than the UEP group (P=0.001). • Patients in the REP group had lower preoperative hematocrit levels than the UEP group (P=0.0001). • Patients in the REP group had a higher preoperative HR than the UEP group (P=0.0001). • There was a significant positive relationship between the amount of fluid recorded on ultrasonography and the frequency of REP (P=0.0001).	High
Darkhaneh et al., 2015 (25)	Iran	247	• UEP: 28.69 (SD = 0.70) • REP: 32.34 (SD = 5.14) • Total: 29.42 (SD = 2.92)	• UEP: 6.92 (SD = 2.39) • REP: 5.70 (SD = 2.38)	N/A	N/A	N/A	79.76/ 20.24	• Patients in the REP group had lower gestational age than the UEP group (P=0. 01). • Patients in the REP group had a higher amount of -hCG than the UEP group (P=0.03). • There was a significant positive relationship between age and REP (P<0.0001).	High
Ashfaq et al., 2017 (22)	Pakistan	80	• UEP: N/A • REP: N/A • Total: 26.12 (SD = 5.38)	N/A	N/A	N/A	N/	A 8.75/ 91.25	• Patients in the REP group had a higher number of parity than the UEP group (P=0.032). • There was a significant negative relationship between age and REP (P=0.039).	High
Anaswara et al., 2021 (21)	India	60	N/A	N/A	N/A	N/A	N/A	41.66/ 58.33	• Patients in the REP group had a higher amount of -hCG than the UEP group (P=0.023). • There was a significant positive relationship between the amount of fluid recorded on ultrasonography and the frequency of REP (P=0.001). • There was a greater risk of REP for ampullar and isthmic pregnancies than other sites of ectopic pregnancies (P=0.001).	High
Bai et al., 2022 (11)	Pakistan	73	• UEP: N/A • REP: N/A • Total: 24.37 (SD = 4.68)	N/A	N/A	N/A	N/A	12.33/ 87.67	Patients in the REP group had a higher number of parity than the UEP group (P=0.039).	High
Li et al., 2022 (32)	Taiwan	225	• UEP: 31.40 (SD = 5.80) • REP: 30.20 (SD = 6.30) • Total: 31.46 (SD = 6.05)	• UEP: 7.10 (SD = 2.60) • REP: 6.10 (SD = 2.40)	N/A	• UEP: 0.90 (SD = 1.20) • REP: 1.40 (SD = 1.30)		21.78/ 78.22	• Patients in the REP group had a higher number of parity than the UEP group (P=0.028). • Patients in the REP group had a lower gestational age than the UEP group (P=0.012). • Patients in the REP group had a higher abdominal pain than the UEP group (P<0.001) • Patients in the REP group had lower preoperative hemoglobin levels than the UEP group (P<0.01).	High

Table 3: Basic characteristics of the included studies in this systematic review and meta-analysis

First Author year	Location	Sample size	Age (year)	Gestational age (weeks)	Gravidity	Parity	Abortion	UEP/REP (%)	Key results	AXIS Score
Sefogah et al., 2022 (3)	Ghana	115	• UEP: N/A • REP: N/A • Total: 27.60 (SD = 5.56)	N/A	N/A	N/A	N/A	28.69/71.31	• The number of REPs was significantly higher in single patients (P=0.01). • There was a greater risk of REP for ampullar pregnancies than other sites of EPs (P=0.01).	High

Data are presented as mean ± standard deviation (SD). REP: Ruptured ectopic pregnancy; UEP: Unruptured ectopic pregnancy; HR: Heart rate; SI: Shock index.

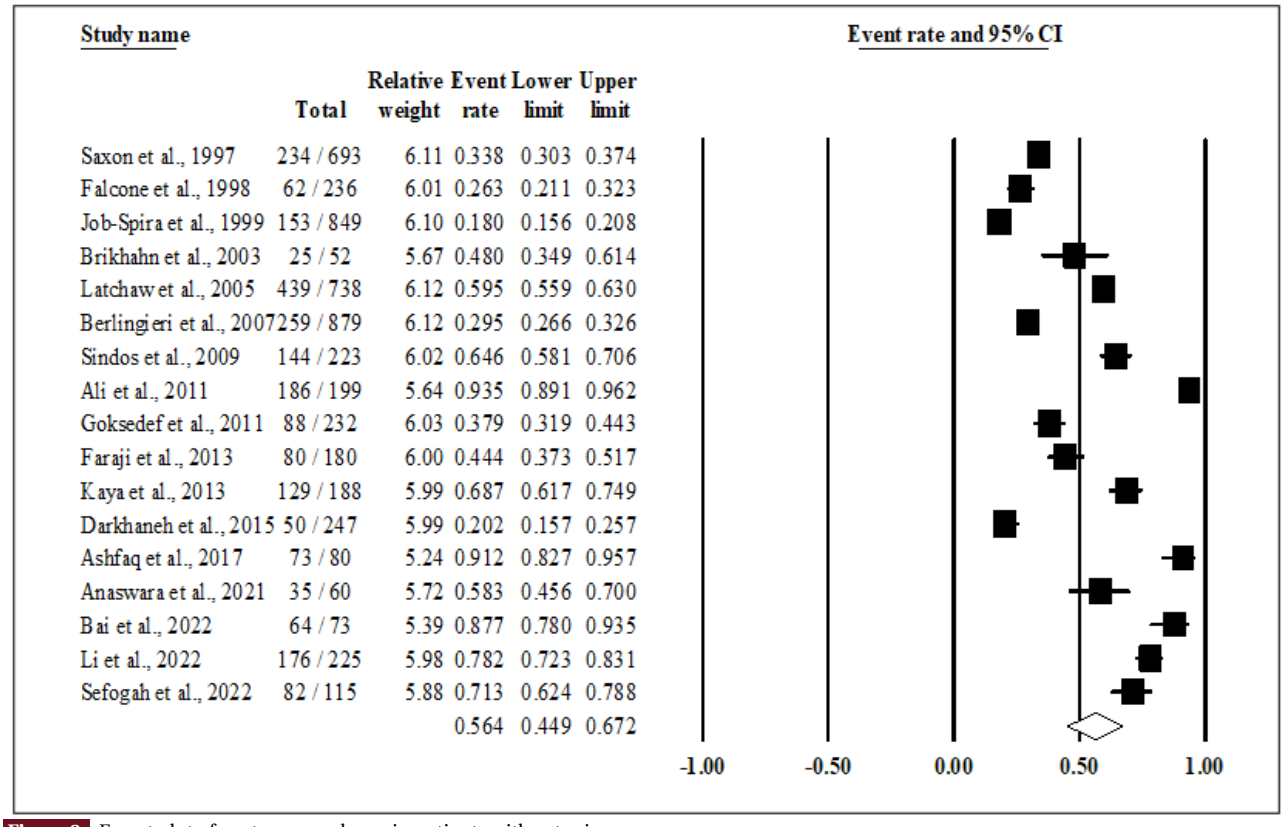

Figure 2: Forest plot of rupture prevalence in patients with ectopic pregnancy.

Table 4: Assessment of the quality of the included articles

Section	Item	Saxon et al., 1997	Falcone et al., 1998	Job-Spira et al., 1999	Brikhahn et al., 2003	Latchaw et al., 2005	Berlingieri et al., 2007	Sindos et al., 2009	Ali et al., 2011	Goksedef et al., 2011	Faraji et al., 2013	Kaya et al., 2013	Darkhaneh et al., 2015	Ashfaq et al., 2017	Anaswara et al., 2021	Bai et al., 2022	Li et al., 2022	Sefogah et al., 2022
Introduction	Clear aims	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
	Appropriate design	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
Methods	Sample size justified	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
	Population defined	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
	Sample representative of population	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
	Selection process representative	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
	Measures to address non-responders	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	Appropriate outcome variables	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
	Valid measures	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
	Defined statistical significance	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
	Methods described	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
Results	Results data described	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
	Concerns about non-response bias	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	Non-responder information described	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	Results internally consistent	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
	Results presented for analyses	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
Discussion	Conclusions justified	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
	Limitations identified	-	-	-	*	-	-	*	*	-	*	-	-	*	-	-	*	*
Others	Funding sources or conflicts of interests	*	*	-	-	-	-	*	-	-	-	-	*	-	-	-	*	*
	Ethical approval/ consent attained	-	-	-	-	–	-	-	*	-	-	-	*	*	*	-	*	*

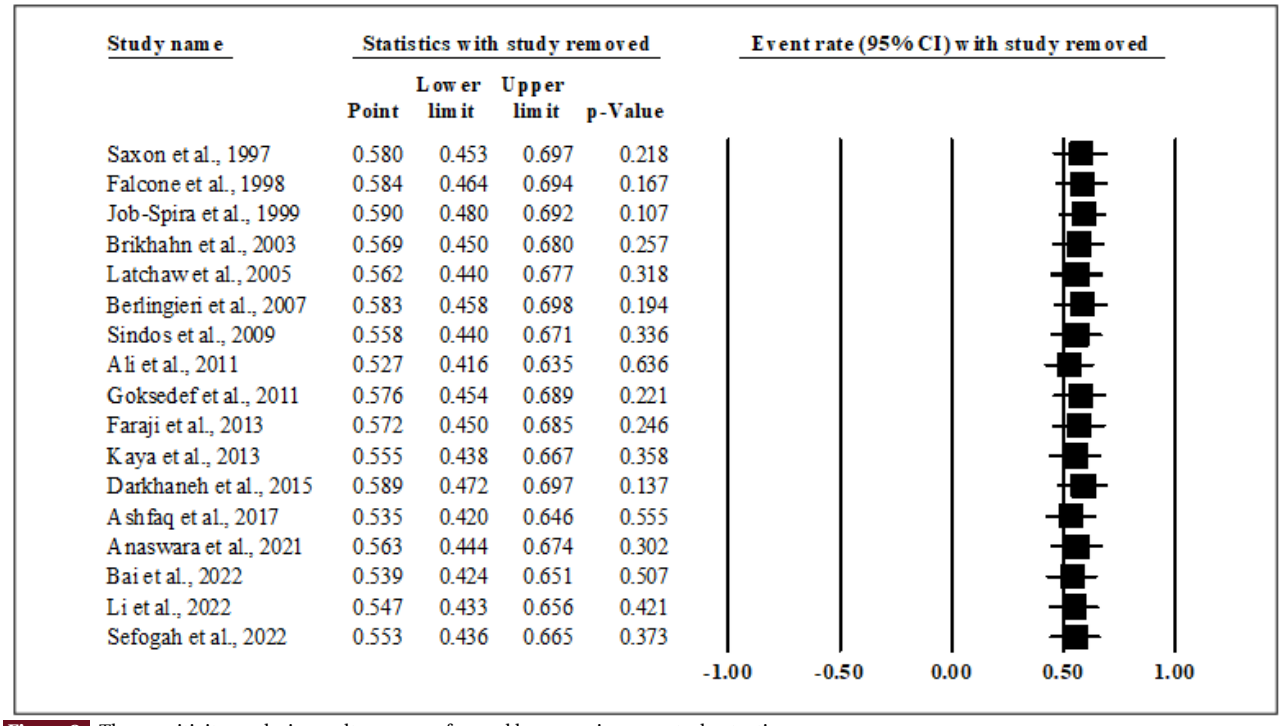

Figure 3: The sensitivity analysis results were performed by removing one study at a time.

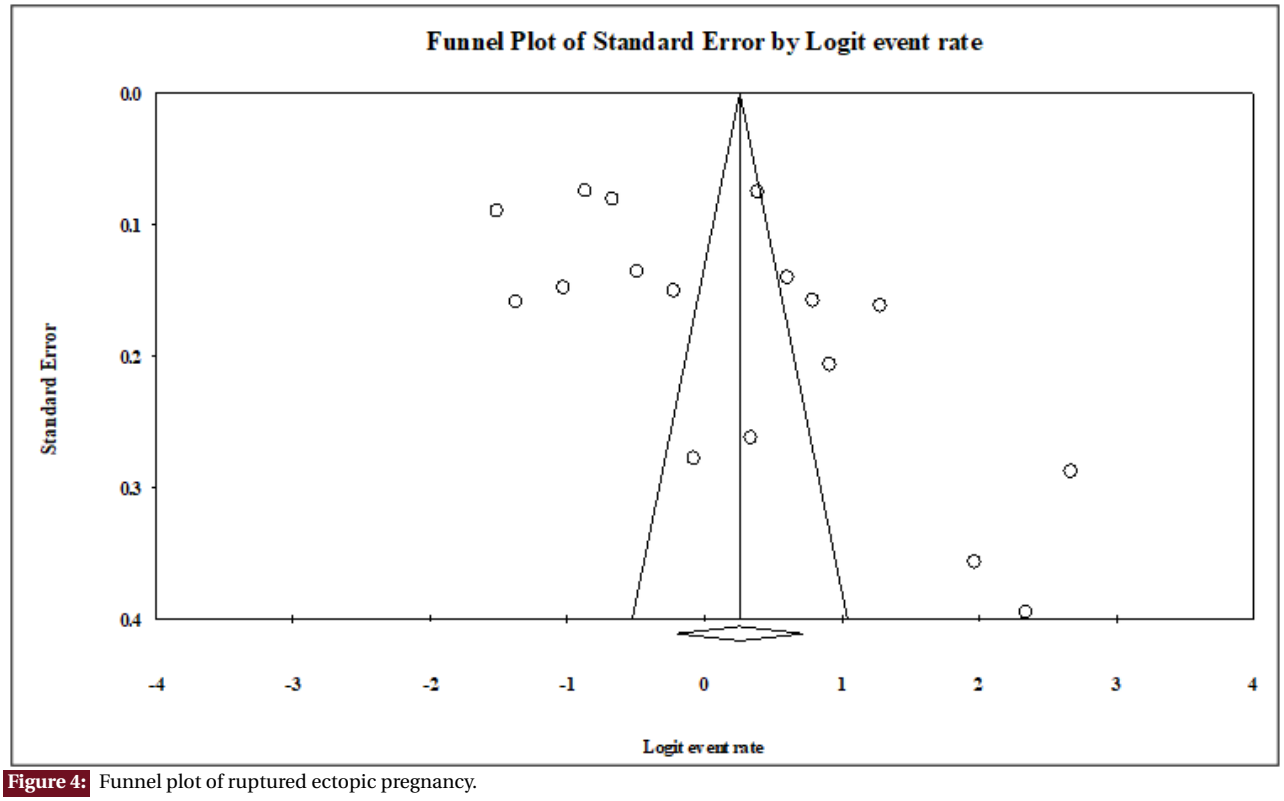

Figure 4: Funnel plot of ruptured ectopic pregnancy.