

# Retrospective Evaluation of the Effect of Age and Obstetric History on Tubal Location in Tubal Ectopic Pregnancies

## Tubal Ektopik Gebeliklerde Yaş ve Obstetrik Öykünün Tubal Yerleşim Üzerine Etkisinin Retrospektif Olarak Değerlendirilmesi

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### Abstract

**Objective:** Ectopic pregnancy is one of the most common early complications of pregnancy. It can cause severe morbidity and even mortality. We aimed to determine the relationship between maternal age, parity, and side of tubal ectopic pregnancy (TEP) in cases with a TEP that underwent surgery.

**Methods:** The present study included 241 patients who were diagnosed with TEP. The side of TEP was determined by laparotomy or laparoscopy. The patients were stratified according to their age as 20-24 years old, 25-29 years old, 30-34 years old, 35-39 years old and  $\geq 40$  years. Besides, the patients were subdivided based on parity as nullipara, primipara, and multipara.

**Results:** The tubal ectopic pregnancies were right-sided in 69.3% and left-sided in 30.7%. Right-sided localization was significantly more common than left-sided localization ( $p < 0.001$ ). When localization of tubal ectopic pregnancies was assessed according to age, it was found that tubal ectopic pregnancies in age groups of 30-34, 35-39, and  $\geq 40$  years were more commonly localized at the right tuba ( $p < 0.001$ ). In age groups of 20-24 and 25-29 years, no significant difference was found in ectopic tubal pregnancy localization.

**Conclusion:** When TEP localization was assessed according to parity, it was found that tubal ectopic pregnancies were more commonly localized at the right tuba in primary and multipara groups.

**Keywords:** Age, ectopic pregnancy, parity, tuba, salpingectomy

### Öz

**Amaç:** Ektopik gebelik, gebeliğin erken komplikasyonlarından biri olup, ciddi morbiditeye ve hatta ölüme neden olabilir. Amacımız, cerrahi uygulanan tubal ektopik gebelik olgularında anne yaşı, doğum sayısı ve tubal ektopik gebeliğin tüp tarafı arasındaki ilişkiyi belirlemektir.

**Yöntem:** Bu çalışma, tubal ektopik gebelik tanısı konulan 241 hastayı içermektedir. Tubal ektopik gebelik tarafı laparotomi veya laparoskopi ile belirlenmiştir. Hastalar, yaşlarına göre 20-24 yaş, 25-29 yaş, 30-34 yaş, 35-39 yaş ve  $\geq 40$  yaş olarak sınıflandırılmıştır. Ayrıca, hastalar doğum sayısına göre nullipara, primipara ve multipara olarak alt gruplara ayrılmışlardır.



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**Öz**

**Bulgular:** Tubal ektopik gebeliklerin %69,3'ü sağ tüpte ve %30,7'si sol tüpte bulunmaktaydı. Sağ tarafta lokalizasyon, sol tarafta lokalizasyondan anlamlı derecede daha yaygındı ( $p<0,001$ ). Tubal ektopik gebelik lokalizasyonu yaş gruplarına göre değerlendirildiğinde, 30-34, 35-39 ve  $\geq 40$  yaş gruplarında tubal ektopik gebeliklerin sağ tüpte daha sık lokalize olduğu bulunmuştur ( $p<0,001$ ). 20-24 ve 25-29 yaş gruplarında ise tubal ektopik gebelik lokalizasyonunda anlamlı bir fark bulunmamıştır.

**Sonuç:** Tubal ektopik gebelik lokalizasyonu doğum sayısına göre değerlendirildiğinde, birinci gebeliği yaşayan ve çoklu doğumu olan gruplarda tubal ektopik gebeliklerin daha sık sağ tüpte lokalize olduğu bulunmuştur.

**Anahtar Kelimeler:** Yaş, dış gebelik, parite, tuba, salpenjektomi

**Introduction**

Ectopic pregnancy can be defined as the implantaion of a fertilized ovum to an area other than the uterus<sup>(1)</sup>. The most common localization of ectopic pregnancy is fallopian tubes, with an incidence of 2% in all pregnancies<sup>(1,2)</sup>. 2.7% of all pregnancy-related deaths are due to ruptured ectopic pregnancy<sup>(3)</sup>. The risk factors for ectopic pregnancy include previous ectopic pregnancy, history of tubal surgery, history of pelvic infection, infertility, pregnancy with assisted-reproductive techniques, smoking, age  $>35$  years, and pregnancy with an intrauterine device; however, there is no identifiable risk factor in almost one-half of women with the diagnosis of ectopic pregnancy<sup>(4,5)</sup>.

Although its contribution to maternal deaths has dramatically decreased in recent years, ruptured ectopic pregnancy remains a significant cause of hemorrhage-related morbidity and mortality resulting from pregnancy in the first trimester<sup>(3)</sup>. The majority of deaths are due to rupture following a non-diagnosed ectopic pregnancy.

Our study aimed to assess whether maternal age and parity are related to tubal ectopic pregnancy (TEP) localization.

**Materials and Methods**

In this study, we retrospectively reviewed data from patients admitted to the obstetric and gynecology clinic and underwent surgery with TEP diagnosis between 2012 and 2016. The Institutional Research Ethics Board approved the applied methods (2017/14-02). Overall, 268 patients who underwent surgery with an initial TEP diagnosis as subsequently proven by histopathological examination were recruited. In comparison, 15 patients with a previous history of surgical and medical treatment for ectopic pregnancy, seven patients who underwent unilateral oophorectomy, and five patients undergoing appendectomy were excluded. These interventions may increase the risk of ectopic pregnancy by leading adhesions. No restriction was defined for maternal

age or gestational age. Thus, data from 241 patients were included in the final analysis.

In all patients, age, gravidity, parity, and surgery mode (laparotomy, laparoscopy) were recorded. The patients were stratified into five groups according to age. The patients were assigned into five groups according to age: group 1, 20-24 years; group 2, 25-29 years; group 3, 30-34 years; group 4 35-39 years; and group 5,  $\geq 40$  years. And three groups according to parity: nullipara, primipara, and multipara.

**Statistical Analysis**

Statistical analyses were performed using SPSS version 20.0. Continuous variables are presented as mean, standard deviation, minimum and maximum values, while categorical variables are presented as frequency. A binominal test was used to compare parity and age groups between groups defined based on localization of ectopic tubal pregnancy. We proposed the null hypothesis that the probability of TEP in the right/left tube is 50%, against the alternative hypothesis that the probability of TEP in the right/left tube is not 50%. A one-way ANOVA test was used to compare the mean age among parity groups. A p-value  $<0.05$  was considered statistically significant.

**Results**

The study included 241 patients who underwent surgery for TEP. The mean age of women was  $33.26\pm 5.3$  years (20-47 years). The mean gravidity was  $2.91\pm 1.4$  (range: 1-8), and the mean parity was  $1.22\pm 0.97$ . All patients underwent Salpingectomy. The Salpingectomy was performed in 164 patients (68%) via laparotomy, whereas in 77 patients (32%) via laparoscopy. Demographic characteristics and surgical techniques were demonstrated in Table 1.

The patients were assigned into five groups according to age: group 1, 20-24 years; group 2, 25-29 years; group 3,

30-34 years; group 4 35-39 years; and group 5,  $\geq 40$  years. TEP was most commonly found in group 3. The right-sided TEP was significantly higher than the left-sided TEP ( $p < 0.01$ ). In group 3, group 4, and group 5 right tuba was significantly more affected than the left tuba ( $p < 0.04$ ,  $p < 0.01$ ,  $p < 0.01$ ). No significant difference was detected in the TEP localization side in groups 1 and 2 ( $p = 0.080$ ,  $p = 0.36$ ) (Table 2).

When patients were subdivided into two groups as age  $< 30$  and age  $\geq 30$  years, it was found that right-sided TEP's were more common in patients aged  $\geq 30$  years. No significant difference was detected in TEP localization in patients aged  $< 30$  years. It was found that right-sided TEP was more common in primary and multipara groups ( $p < 0.005$ ). When the age of parity groups was assessed, the mean age was  $31.1 \pm 5.51$  years in the nullipara group,  $33.38 \pm 5.34$  years in the primipara  $34.60 \pm 4.93$  years in the multipara group (Table 3).

**Table 1. Demographic characteristics and surgical procedures**

Variable	Mean, min-max, SD, n, %
Age	33.26 $\pm$ 5.3 (20-47)
Gravida	2.91 $\pm$ 1.4 (1-8)
Parity	1.22 $\pm$ 0.97
Laparotomy	164 (68%)
Laparoscopy	77 (32%)

Min-max: Minimum-maximum, SD: Standard deviation

## Discussion

In our study, we observed that TEP more commonly develops in the right tube. Although the localization of TEP (right or left tube) has been investigated in many studies, the cause of this localization has not been evaluated so far. Some studies have reported that TEP is more commonly localized in the right tube, while others have reported that the left tube is a more common localization for TEP<sup>(6,7,8,11)</sup>. In the existing literature, there are two studies focused on TEP localization. One of these studies reported that TEP is more commonly seen in the right tube, while the other study did not find a significant difference in TEP localization but observed that it is slightly more common in the right tube<sup>(12,13)</sup>.

In our study, when TEP localization was assessed according to age groups, it was found that there was no significant difference between groups 1 and 2, although TEP was more commonly seen on the right side. However, it was seen that TEP was more commonly localized at the right tuba in groups 3, 4, and 5 ( $p < 0.05$ ). In a recent study including 6,186 patients, it was found that TEP was more commonly localized at the right tuba in age groups of 20-24 years, 25-29 years, and 30-34 years, while there was no significant difference in age groups of 30-34 and 35-39 years regarding TEP localization<sup>(12)</sup>. In another study, including 120 patients, TEP localization was assessed according to age groups. It was found that TEP was more commonly localized at right

**Table 2. The prevalence of TEP and affected tubal portion according to women's age**

Variable	Classification	n, %	Right side TP n, %	Left side TP n, %	p-value
Age	Group 1. 20-24	16 (6.64%)	9 (3.73%)	7 (2.91%)	0.80
	Group 2. 25-29	43 (17.84%)	25 (10.37%)	18 (7.47%)	0.36
	Group 3. 30-34	76 (31.53%)	48 (19.91%)	29 (12.62%)	0.04
	Group 4. 35-39	74 (30.7%)	58 (24.06%)	16 (6.64%)	<0.001
	Group 5. $\geq 40$	31 (12.86%)	27 (11.2%)	4 (1.66%)	<0.001
<b>Total</b>	241	241	167 (69.3%)	74 (30.7%)	<0.001

TEP: Tubal ectopic pregnancy

**Table 3: Comparison of ectopic pregnancy site according to parity groups**

Variable	Classification	Age mean, SD	Right side TEP, (n)	Left side TEP, (n)	Total (n, %)	p-value
Parity	Nulliparous	31.1 $\pm$ 5.51	37	23	60 (24.9%)	0.092
	Primiparous	33.38 $\pm$ 5.34	59	35	94 (39%)	0.017
	Multiparous	34.60 $\pm$ 4.93	69	18	87 (36.1%)	<0.001

SD: Standard deviation, TEP: Tubal ectopic pregnancy

tuba in age groups 30-34 and 35-39 years while there was no significant difference in age groups 20-24, 25-29, and >40 years, regarding TEP localization<sup>(13,16)</sup>.

Although ectopic pregnancy incidence is increased by advancing age<sup>(14)</sup>, it is most frequently seen between 30 and 34 years of age<sup>(12,13)</sup>. Our findings are in agreement with the literature. When a relationship between TEP and parity was assessed, there are contradictory results in the literature. Most studies reported that TEP most commonly occurred in multipara pregnancies<sup>(6,9,10)</sup>; however, in the most extensive series, including 6,186 cases, it was reported that TEP was most commonly detected in nullipara pregnancies<sup>(12)</sup>. In our study, the rate of TEP was observed to be highest in multiparous women, while it was observed to be the lowest in nulliparous women.

In studies investigating the effects of parity on TEP localization, it was found that TEP was more commonly seen in the right tuba in nullipara cases. Also, there was no significant difference in primipara and multipara cases regarding TEP localization<sup>(12)</sup>. In our study, no significant difference was detected in nullipara cases regarding TEP localization, while TEP was found to be more commonly localized at the right tuba in primipara and multipara cases ( $p < 0.05$ ). This may be due to the younger age of nullipara cases compared to primipara and multipara cases in our study.

While the mechanisms explaining the more common localization of TEP in the right tube remain unclear, we believe that there may be three mechanisms involved in this localization:

1. Ovulation predominantly occurs at one side
2. Higher fertilization potential of oocytes at one side
3. Insufficient transport function of one tuba compared to other

A study on the ovulation side reported that ovulation at the right side was seen in 55% of >2,000 fertile and infertile cycles<sup>(15)</sup>. The evidence may explain right-sided dominance in TEP. Although ovulation characteristics were assessed in the study, as mentioned earlier, the relationship between age and side of ovulation was not considered. In another study, 2,090 natural cycles in the right and left ovaries were assessed according to age. The authors reported that ovulation occurs more commonly in the right ovary in all age groups between 20 and 50. In our study, right-sided TEP

dominancy was observed in patients aged >30 years, while no significant difference was observed in those aged <30 years. This may be due to the limited sample size in our study.

The right-sided TEP localization becomes more common by advancing age; this may be due to variation in oocytes' fertilization potentials. This may also be due to differences in vascularity of ovaries. The ampulla and fimbria of the tube are supplied by branches of the ovarian artery, and these branches may supply the whole tube<sup>(17)</sup>. Areas of contact between the ovarian artery and vein are characterized by a thinning of the ovarian vein wall<sup>(18)</sup>, and it is believed that there is a countercurrent from the ovarian veins to the arteries<sup>(19)</sup>. Fukuda et al.<sup>(15)</sup> suggested that the rate of right-sided ovulations is around 55%, which is in accordance with our study. The right-sided dominance of TP may result from the right-sided dominance of ovulation. It could also be explained by vascular differences between the 2 ovaries: The junction between the left ovarian and renal veins is generally more perpendicular than that between the right ovarian vein and vena cava. However, the underlying mechanism is unclear.

Pelvic infections, endometriosis, and hormonal factors may lead to TEP by influencing the tuba's anatomy and functions<sup>(20)</sup>. There is a need for further studies to investigate variations in the transport capacity of fallopian tubes.

Our study showed that right-sided TEP is significantly more common than left-sided TEP.

In conclusion, the left-right asymmetries of TP include right-sided dominance and the clinical feature differences between the 2 sides of TP. Although the occurrence of right-sided TP is more common than the left side. As such, if these findings are confirmed in other studies, consideration should be given to a more aggressive approach to right-sided EPs. These findings may be due to a higher frequency of right-sided ovulations and anatomic differences between the 2 fallopian tubes. However, the underlying mechanisms are still unknown. There appear to be differences in right versus left dominance in a variety of gynecologic conditions. Increased knowledge of the pathophysiology and predisposing conditions may help improve treatment strategies and earlier diagnosis. Furthermore, increased maternal age and parity increase the likelihood of involvement of the right tube. However, no definitive conclusion can be drawn regarding underlying mechanisms. We think that the right adnexal region should be evaluated in detail after assessing the pelvis by TVUSG in non-diagnostic cases.

The patients were stratified according to their age as 20-24 years old, 25-29 years old, 30-34 years old, 35-39 years old and  $\geq 40$  years.

## Ethics

**Ethics Committee Approval:** This study was approved by University of Health Sciences Turkey, İzmir Tepecik Training and Research Hospital (2017/14-02).

**Informed Consent:** Parents were asked to fill in a 25-question google questionnaire.

**Peer-review:** Externally peer-reviewed.

## Authorship Contributions

Surgical and Medical Practices: O.Ö., Concept: F.Ö., Design: E.K., S.Y.K., Data Collection or Processing: O.Ö., Analysis or Interpretation: İ.G., S.Y.K., Literature Search: H.İ., Writing: E.K.

**Conflict of Interest:** No conflict of interest was declared by the authors.

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