

# Risk Factors for Recurrent Ectopic Pregnancy: A Case - Control Study

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**OBJECTIVES:** To investigate the role of epidemiological factors in recurrent ectopic pregnancies.

**STUDY DESIGN:** From January 2003 to February 2005, 205 women with single ectopic pregnancy and 20 women with recurrent ectopic pregnancy were identified. The information collected for each woman included socio-demographic characteristics, smoking status, reproductive, sexual, contraceptive and medical histories (including PID).

**RESULTS:** The risk of recurrent ectopic pregnancy was increased with age, mean of gravidity and history of pelvic surgery. After multivariate analysis, there was no significant association between recurrent ectopic pregnancy and any variables.

**CONCLUSION:** Primary prevention of ectopic pregnancy is the best measure against preventing recurrent ectopic pregnancy. Moreover, for successful secondary prevention, identification of modifiable risk factors for recurrent ectopic pregnancy is important.

**Key Words:** Ectopic pregnancy, Epidemiology, Recurrent, Risk factors

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## Introduction

Ectopic pregnancy accounts 1-2% of all pregnancies and it is a considerable cause of maternal morbidity and mortality.<sup>1</sup> The estimated recurrence risk of ectopic pregnancy ranges from 10-27%, a fivefold to 10-fold increase over the general population risk.<sup>2,3,4</sup> Information derived from epidemiologic studies, which compare risk factors of patients between recurrent ectopic pregnancy and single ectopic pregnancy could help clinicians to counsel patients before a recurrence occur. Therefore, we designed a study to investigate the role of epidemiological factors in recurrent ectopic pregnancy.

## Material and Method

From January 2003 to February 2005, 205 women with

single ectopic pregnancy and 20 women with recurrent ectopic pregnancy, whose diagnosis had been confirmed by histopathological examination were identified. This study was approved by Zekai Tahir Burak Women Health Education and Research Hospital ethical review board and was designed in accordance with the Declaration of Helsinki.

The information collected for each woman (from face to face interview) included socio-demographic characteristics, smoking status, reproductive, sexual, contraceptive and medical histories (including PID).

### Statistical methods

Data were stored and analyzed using SPSS (Statistical Package for Social Science; release 11.0) in an IBM-compatible computer and expressed as means  $\pm$  SD. Differences between means were compared by Student's t test for parametric data sets and Mann-Whitney U test for nonparametric data sets. Odds ratio (OR) and 95 percent confidence intervals (CI) were used to describe the association risk factors and recurrence. Multivariable modeling was employed to determine which characteristics were associated with EP. In this model we included only variables, which were associated with the risk of ectopic pregnancy in univariate analysis. Statistical significance was set at  $p < 0.05$ .

## Results

The risk factors for recurrent ectopic pregnancy are listed in table 1. Patients with recurrent ectopic pregnancy were more likely older than single ectopic pregnancy (mean age:

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33.9± 5.5, 30.0 ± 5.8 years, respectively;  $p= 0.005$ ). The mean number of pregnancies was significantly higher in women with recurrent ectopic pregnancy than primary ectopic pregnancy ( $p=0.003$ ). A history of pelvic surgery was significantly

higher in patients with recurrent ectopic pregnancy than single ectopic pregnancy (OR:10.6; 95% CI:3.4-33.2;  $p<0.001$ ). After multivariate analysis, there was no significant association between ectopic pregnancy and any variables.

*Table 1: Socio-demographic characteristics, cigarette smoking, obstetrical, surgical and gynecological history and contraceptive practices of women with primary and recurrent ectopic pregnancy*

Variables	Primary ectopic pregnancy (n=205) N(%)	Recurrent ectopic pregnancy (n=20) N(%)	Crude OR	95% CI	p
Age (mean ± SD)	30.0 ± 5.8	33.9 ±5.5			0.005
Woman's age (years)					
<35	153 (74.6)	10 (50.0)	1.0		
≥35	52 (25.4)	10 (50.0)	2.9	1.2-3.2	0.02
Marital status					
Single / separated	9 (4.4)	1 (5.0)	1.0		
Married	196 (95.6)	19 (95.0)	0.9	0.1-7.3	1.00
Occupation					
Housewife	168 (82.0)	15 (75.0)	1.0		
Worker	37 (18.0)	5 (25.0)	1.5	0.5-4.4	0.55
Family income (YTLa)					
<1000	139 (67.8)	11 (55.0)	1.0		
≥1000	40 (19.5)	4 (20.0)	1.3	0.4-4.2	0.75
Unknown	26 (12.7)	5 (25.0)			
Years of schooling					
<5	111 (54.0)	9 (45.0)	0.7	0.3- 2.1	0.60
6-11	64 (31.2)	7 (35.0)	1.0		
>12	26 (12.7)	4 (20.0)	1.4	0.4- 5.2	0.73
Smoking					
Never	108 (52.7)	8 (40)	1.0		
Past smoker	20 (9.7)	1(5)	0.6	0.1-5.7	1.00
Current Smoker	77 (37.6)	11 (55)	1.9	0.7-5.0	0.17
Gravidity (mean±SD)	2.3±1.8	3.7 ±2.0			0.003
Prior deliveries					
None	50 (24.4)	3 (15.0)	1.0		
≥1	155 (85.6)	17 (85.0)	1.8	0.5-6.5	0.42
Prior spontaneous abortions					
None	163 (79.5)	17 (85.0)	1.0		
≥1	42 (20.5)	3 (15.0)	0.7	0.2-2.4	0.77
Prior induced abortions					
None	141 (68.8)	11 (55.0)	1.0		
≥1	64 (31.2)	9 (45.0)	1.8	0.7-4.6	0.21
Prior pelvic surgery <sup>b</sup>					
No	149 (72.7)	4 (20.0)	1.0		
Yes	56 (27.3)	16 (80.0)	10.6	3.4-33.2	0.0001
Prior cesarean section					
No	162 (79.0)	17 (90.0)	1.0		
Yes	43 (21.0)	3 (10.0)	0.4	0.1-1.9	0.38
Appendectomy					
No	201 (98.0)	18 (90.0)	5.6	0.9-32.6	0.09
Yes	4 (2.0)	2 (10.0)	1.0		
Age at menarche (years)					

≤13	111 (54.1)	8 (40.0)	1.0		
>13	82 (40.0)	12 (60.0)	2.0	0.8- 5.2	0.13
Unknown	12				
Age at first intercourse (years)					
<20	111 (54.4)	10 (50.0)	1.0		
≥20	93 (45.6)	10 (50.0)	1.2	0.5-3.0	0.71
Lifelong no of sexual partner					
1	183 (90.0)	19 (95.0)	1.0		
>1	20 (10.0)	1 (5.0)	0.5	0.1-3.8	0.70
Vaginal douching					
No	102 (49.8)	11 (55.0)	1.0		
Yes	103 (50.2)	9 (45.0)	0.8	0.3-2.0	0.65
Prior PIDc					
No	176 (85.9)	19 (95.0)	1.0		
Yes	29 (14.1)	1 (5.0)	0.3	0.1-2.5	0.49
History of infertility					
No	153 (74.6)	15 (75.0)	1.0		
Yes	51(24.9)	5 (25.0)	1.0	0.3-2.9	1.00
Contraception at the time of conception					
No	103 (50.2)	14 (70.0)	1.0		
Yes	102 (49.8)	6 (30.0)	0.4	0.2-1.2	0.09
Tubal ligation					
No	202 (98.5)	19 (95.0)	1.0		
Yes	3(1.5)	1 (5.0)	3.5	0.3-35.8	0.31
Intrauterine device					
No	133 (64.9)	17 (85.0)	1.0		
Yes	52 (25.4)	3 (15.0)	0.5	0.1-1.6	0.29
Missing	20				
Condom, Spermisid					
No	192	(93.6)	20	(100.0)	- 0.61
Yes	13	(6.3)	0		

a:1\$=1.57 TL, 1€=2.2 TL, b: Including any surgery for the treatment EP, c: PID, association of fever, abdominal pain and vaginal discharge

## Discussion

Primary prevention of ectopic pregnancy is the best measure against preventing recurrent ectopic pregnancy. Moreover, for successful secondary prevention, identification of modifiable risk factors for recurrent ectopic pregnancy is important. In the present study, we found that risk for recurrent ectopic pregnancy increases with maternal age. Butts et al.<sup>5</sup> found that age did not differ significantly between the two groups except the category 'less than twenty', which contained great percentage of patients who had single ectopic pregnancy than recurrent ectopic pregnancy (OR=0.08, p=0.02).

We found no significant difference between the groups for pelvic inflammatory disease (PID) history. In agreement with our study, Butts et al.<sup>5</sup> found no significant difference between the groups in terms of gonorrhoea, chlamydia or PID, either

historically or at the time of diagnosis. In contrast, Skjeldestad et al<sup>2</sup> found that history of treatment for PID and infectious tubal stigmata (adhesions and macroscopic tubal damage) visualized at surgery for initial ectopic pregnancy have been strongly associated with recurrent ectopic pregnancy.<sup>2</sup> In the same study, the risk for recurrence of ectopic pregnancy was associated with age at first ectopic pregnancy occurred, initiation of infertility work-up and conception with an intrauterine device at index pregnancy. In agreement with the result of our study, they found no association between recurrent ectopic pregnancy and marital status, history of spontaneous or induced abortion and appendectomy.<sup>2</sup>

Our data demonstrated that women with a history of pelvic surgery have increased risk of recurrent ectopic pregnancy. In agreement with our study, Butts et al.<sup>5</sup> found that patients with recurrent ectopic pregnancy have a higher rate of history of

pelvic surgery. Moreover, in contrast to our study they identified association between the history of live birth and history of spontaneous miscarriage.<sup>5</sup>

An important limitation of our study was that, our sample size was limited, especially in the recurrent ectopic groups. Large prospective cohort studies are necessary to elucidate the risk factors for recurrent ectopic pregnancy.

### **Tekrarlayan Dış Gebelik Vakalarında Risk Faktörleri: Vaka Kontrol Çalışması**

**AMAÇ:** Tekrarlayan dış gebelikte epidemiyolojik risk faktörlerinin araştırılması.

**GEREÇ VE YÖNTEM:** Ocak 2003 ile Şubat 2005 yılları arasında 205 ilk defa dış gebelik tanısı konan vakalarla aynı zaman diliminde tekrarlayan dış gebelik tanısı konan vakalar belirlendi. Her kadına ait sosyodemografik, sigara alışkanlık durumu, üreme, seksüel, kontraseptif ve medikal özgeçmişleri (geçirilmiş pelvik enflamatuvar hastalık dahil) saptandı.

**BULGULAR:** Tekrarlayan dış gebelik riskinin yaşla, ortalama gravida sayısı ve geçirilmiş pelvik enfeksiyon öyküsü ile arttığı saptanmıştır. Çok değişkenli analiz sonrası ise tekrarlayan dış gebelikte herhangi bir değişken arasında herhangi bir ilişki saptanmamıştır.

**SONUÇ:** Tekrarlayan dış gebelikten korunma için en önemli faktör primer korunma olarak görülmektedir. İlave olarak sekonder korunma için tekrarlayan ektopik gebeliklere ait modifiye edilebilir risk faktörlerinin belirlenmesi önemli olacaktır.

**Anahtar Kelimeler:** Dış gebelik, Epidemiyoloji, Tekrarlayan, Risk faktörleri

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