

# Risk Factors of Ectopic Pregnancy

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## Abstract

**Objectives :** To assess the risk factors of ectopic pregnancy in Thai women.

**Setting :** Department of Obstetrics and Gynaecology, Faculty of Medicine, Chulalongkorn University.

**Design :** Case controlled study.

**Material and Method :** From 1999 to 2000, 208 cases of ectopic pregnancy and 781 controls (postpartum women) were included in the study. The women were interviewed by trained research interviewers using a standardized questionnaire. Detailed information regarding age at first intercourse, number of sexual partners, history of changing partners within 6 months, previous obstetric history, history of spontaneous and criminal abortion, history of pelvic inflammatory disease, smoking, history of endometriosis and history of previous ectopic pregnancy was collected.

**Results :** By multivariate analysis, 5 variables remained as strong and independent risk factors for ectopic pregnancy : the number of sexual partners  $\geq 2$  (OR = 3.02, 95% CI (1.75-5.23), vaginal delivery  $\geq 1$  (OR = 0.005, 95% CI (0.002-0.0015), history of pelvic inflammatory disease (OR = 3.17, 95% CI (1.40-7.19), smoking (OR = 2.49, 95% CI (1.36-4.55), infertility (OR = 2.74, 95% CI (1.35-5.54)).

**Conclusion :** Problems of multiple sexual partners, pelvic inflammatory disease, smoking and infertility were the main risk factors of ectopic pregnancy in Thai women.

**Key word :** Risk Factors, Ectopic Pregnancy

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Ectopic pregnancy is an important cause of maternal death and is an increasing health problem (1-5). Prompt diagnosis and treatment are the key in saving maternal life. Even if there was had the progression in earlier diagnosis, conservative and medical treatment, ectopic pregnancy still remain the cause of maternal death during the first trimester of pregnancy in industrial countries(6,7). The incidence of ectopic pregnancy in Thailand is different in each center. At King Chulalongkorn Memorial Hospital, the incidence is 1 per cent of patients attending the out patient clinic or 3.7 per cent of first trimester abortions(8). There are many reports of the risk factors of ectopic pregnancy such as: history of previous ectopic pregnancy, history of pelvic inflammatory disease and history of criminal abortion, etc(9-18). Up to now, there has been no report of ectopic pregnancy in Thailand from different ethnic groups, culture and life styles. The purpose of this study was to identify the risk factors of ectopic pregnancy in Thai women which might be useful in selecting patients at risk and planning a prevention program for the future.

## MATERIAL AND METHOD

From 1999 to 2000, 208 cases of ectopic pregnancy diagnosed by laparoscopy or laparotomy and confirmed by pathology at King Chulalongkorn Memorial Hospital were included in the study. The control groups included women who gave birth at term (more than 37 weeks' gestation) to healthy infants on randomly selected days at the same hospital. The control subjects were chosen within 1 week of case ascertainment. A total of 781 controls were interviewed. The ratio of one case to four controls was chosen for cost/efficacy considerations, particularly because cases of ectopic pregnancy were relatively rare.

Fifty controls were lost due to administrative problems and some of them were not eligible for the inclusion criteria. Trained interviewers used a standard questionnaire to obtain information on the personal characteristics, gynecologic and obstetrics history. The factors included in the questionnaires were: the number of sexual partners, age at first sexual intercourse, changing of sexual partners within 6 months, obstetrics history, history of pelvic inflammatory disease (PID) (diagnosed and treated by a physician), smoking  $\geq 1$  cigarette/day, endometriosis (diagnosed and treated by physician), previous ectopic

pregnancy, infertility (no conception within 1 year after marriage).

## Statistical analysis

The statistical analysis was performed using SPSS version 10.0 for microsoft window 2000. Chi square test was used for the categorical data. Unpaired student *t*-test was used in the continuous data. The correlations between variables and ectopic pregnancy were determined by stepwise logistic regression. The estimated partial odds ratios and 95 per cent confidence intervals of each risk factors were computed by taking the exponent of the product of its coefficient in the logistic regression with the difference within the variables.

## RESULTS

There was no statistical difference of age, religion, profession and education in both groups (Table 1). After univariate analysis, all the 11 variables were different statistically except for the first age at first sexual intercourse (Table 2). When using stepwise multiple logistic regression, the number of sexual partners  $> 2$ , history of PID, smoking and infertility were shown to be risk factors of ectopic pregnancy (Table 3).

## DISCUSSION

From the present study, the authors found that multiple sexual partners, history of pelvic inflammatory disease, smoking and infertility were strong risk factors and previous vaginal delivery to be the protective factor. The present findings were largely in agreement with the published literature on risk factors for ectopic pregnancy. Pelvic inflammatory disease (PID) can damage tubal function and tubal anatomy. Behavioral factors like multiple sexual partners lead to higher chance of having PID. There are many reports of PID being caused by Chlamydia Trachomatis as a strong risk factor(17,19). The authors did not have detailed data available for this type of organism. The diagnosis of chlamydial infection requires a special technique such as antigen detection or special culture. The present result was consistent with many previous reports (the odds ratio ranging between 2.0 and 7.5)(5,12,13,15,16).

Smoking can reduce the motility of the tubes, as nicotine has an adverse effect on ciliary motion (19, 20). Nicotine has also been shown to delay ovum

entry into the uterus as well as blastocyst formation and implantation. The authors found a strong relationship similar to previous reports with an odds ratio of 1.3-2.3(12,14). Infertility was another strong risk fac-

tor as in many previous reports (odds ratio of 2.6-4.0)(10,11,13). Tubal damage from surgery, infection, or endometriosis may cause infertility and lead to ectopic pregnancy. A similar finding was related to a

**Table 1. Patients' characteristics.**

	Ectopic pregnancy N = 208 Mean $\pm$ SD		Controls N = 781 Mean $\pm$ SD		Statistical difference
	N	%	N	%	
Age (yrs)	27.8 $\pm$ 6.3		25.2 $\pm$ 5.4		NS
Religion					
Buddhism	201	97.4	773	98.3	NS
Christian	1	0.3	4	0.5	NS
Islam	6	2.3	9	1.1	NS
Profession					
Housewife	68	32.7	361	46.2	NS
Employee	113	54.3	358	45.9	NS
Business	18	8.7	51	6.5	NS
Government officer	3	1.4	6	0.8	NS
Agriculture	3	1.4	6	0.8	NS
Student	3	1.4	2	0.2	NS
Education					
None	4	1.9	13	1.7	NS
$\leq$ Secondary school	167	80.29	690	88.4	NS
Vocational school	21	10.1	62	7.9	NS
Bachelor degree	16	7.7	17	2.2	NS

NS = not significant

**Table 2. Univariate analysis of selected factors among cases and controls.**

Factors	Ectopic pregnancy N = 208 Mean $\pm$ SD		Controls N = 781 Mean $\pm$ SD		Statistical difference
	N	%	N	%	
Age at first sexual intercourse	20.24 $\pm$ 4.24		19.77 $\pm$ 3.42		NS
Number of sexual partners $\geq$ 2	58	27.88	81	10.37	p = 0.014
Changing partners within 6 months	5	2.4	3	0.38	p < 0.0001
Previous obstetrics history					
Vaginal delivery $\geq$ 1	103	49.52	774	99.10	p < 0.0001
Cesarean Section $\geq$ 1	10	4.81	6	0.77	p < 0.0001
Spontaneous abortion $\geq$ 1 time	17	8.17	65	8.32	NS
Criminal abortion $\geq$ 1 time	36	17.31	69	8.83	p < 0.0001
History of pelvic inflammatory disease	24	11.52	27	3.46	p < 0.0001
Smoking	39	18.75	70	8.96	p < 0.0001
History of endometriosis	2	0.96	0	0	p = 0.007
Previous ectopic pregnancy	59	28.36	4	0.51	p = 0.0001
History of infertility	48	23.07	44	5.63	p $\leq$ 0.0001

NS = not significant

**Table 3. Multivariate analysis.**

Factors	Odd ratio	95% CI
Sexual partners $\geq 2$	3.02	1.75-5.23
Vaginal delivery $\geq 1$	0.005	0.002-0.015
History of pelvic inflammatory disease	3.17	1.40-7.19
Smoking	2.49	1.36-4.58
Infertility	2.74	1.35-5.54

previous successful vaginal delivery as it appears to have a protective effect. The authors did not find any increased risk factors of ectopic pregnancy with a history of spontaneous abortion as in many previous reports(5,13). Criminal abortion was not found to be a risk factor after multivariate analysis. (Table 3) Criminal abortion may be associated with other risk factors such as multiple sexual partners but it was not

the main risk factor by itself. The authors did not observe any association between maternal age and ectopic pregnancy as the ages of cases and control were not different.

The present study showed that ectopic pregnancy was associated with different risk factors. This was the first study in Thailand which was designed as a hospital based study. A population-based case-controlled study is recommended. Long-term studies to confirm the reduction in risk provided by cessation of these factors before conception are also suggested.

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#### REFERENCES

1. Beral V. An epidemiological study of recent trends in ectopic pregnancy. *Br J Obstet Gynaecol* 1975; 82: 775-82.
2. Westrons I, Bengtsson LPH, Mardh PA. Incidence, trends and risk of ectopic pregnancy in a population of women. *BMJ* 1981; 282: 15-18.
3. Shiiona PH, Harlap S, Pellegrin F. Ectopic pregnancies: Risking incidence rates in Northern California. *Am J Public Health* 1982; 72: 173-5.
4. Centers for Disease Control. Ectopic pregnancy United States. 1981-1983. *MMWR* 1986; 35: 289-91.
5. Chow WH, Daling JR, Cates W Jr, et al. Epidemiology of ectopic pregnancy. *Epidemiol Rev* 1987; 9: 70-94.
6. Atrash IIK, Hughes JM, Hogue CJR. Ectopic pregnancy in the United States. 1970-1983. CDC surveillance summaries, *MMWR* 1986; 35: 29-37.
7. Chavkin W. The rise of ectopic pregnancy. Exploration of possible reasons. *Int J Gynaecol Obstet* 1982; 20: 341-50.
8. Annual statistics. Department of Obstetrics and Gynecology, Faculty of Medicine, Chulalongkorn University. Bangkok: Department of Obstetrics and Gynecology; 2001.
9. Howard WO. Ectopic pregnancy and Intrauterine contraceptive devices : New perspectives. *Obstet Gynecol* 1981; 57: 137-44.
10. Polly AM, John FA, Carolyn BC, Janette HS, Lconard TK. Risk factors for ectopic pregnancy. *JAMA* 1988; 259: 1823-7.
11. Nordenskjold F, Mats A. Risk factor for ectopic pregnancy. *Acta Obstet Gynecol Scand* 1991; 70: 575-9.
12. Joël Coaste, Nadine Job-spira, Herve F, Emile P, Alfed S. Risk factors for ectopic pregnancy : A case-control study in France, with special focus on infectious factors. *Am J Epidemiol* 1991; 138: 311-4.
13. Kalandid A, D M, Tzonou A, Hsieh CC, Aravandions D, Trichopoulos D. Induced abortions, contraceptive practices, and tobacco smoking as risk factors for ectopic pregnancy in Athens, Greece. *Br J Obstet Gynaecol* 1991; 98: 207-13.
14. Stergachis A, Scholes D, Daling JR, Weiss NS, Chu J. Maternal cigarette smoking and the risk of tubal pregnancy. *Am J Epidemiol* 1991; 133: 332-7.
15. Parazzini F, Tozzi L, Ferraroni M, Bocciolone L, Vecchia CL, Fedle L. Risk factors for ectopic pregnancy: An Italian case-control study. *Obstet Gynecol* 1992; 80: 821-5.

16. Cost J, Collet P, Laumon B, Job-spira N, Bremond C. Sexually transmitted diseases as major causes of ectopic pregnancy : Results from a large case-control study in France. *Fertil and Steril* 1994; 62: 289-95.
17. Phillips RS, Tuomala RE, Feldblum PJ, et al. The effect of cigarette smoking, chlamydia trachomatis infection, and vaginal douching on ectopic pregnancy. *Obstet Gynecol* 1992; 79: 85-90.
18. Basuki B, Rossing Ma, Daling JR. Intrauterine device use and risk of tubal pregnancy : An Indonesian case-control study. *Int J Epidemiol* 1994; 23: 1000-5.
19. Chow JM, Yonckura L, Richwald GA, et al. The association between chlamydia trachomatis and ectopic pregnancy. A matched-pair case-control study. *JAMA* 1990; 263: 3164-7.
20. Handler A, Davis F, Ferre C, Yeko T. The relationship of smoking and ectopic pregnancy. *Am J Public Health* 1980; 79: 123-42.

## ปัจจัยเสี่ยงต่อการตั้งครรภ์นอกมดลูก

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วัตถุประสงค์ : เพื่อศึกษาปัจจัยเสี่ยงของการตั้งครรภ์นอกมดลูกในสตรีไทย

สถานที่ : ภาควิชาสูติศาสตร์-นรีเวชวิทยา, คณะแพทยศาสตร์ จุฬาลงกรณ์มหาวิทยาลัย

รูปแบบการศึกษา : Case control

วัสดุและวิธีการ : ระหว่างปี 2542-2543 ได้ทำการศึกษาในผู้ป่วยตั้งครรภ์นอกมดลูกจำนวน 208 ราย (Cases) และสตรีหลังคลอดบุตร 781 ราย (Controls) โดยผู้ป่วยจะได้รับการอบรมเป็นปัจจัยเสี่ยงต่าง ๆ ดังนี้ อายุเมื่อมาเพคลัมพันธ์ครั้งแรก จำนวนคุณอนที่ผ่านมา จำนวนคุณอนในรอบ 6 เดือน ประวัติการแท็บบูตรองหรือการทำแท็บดูกูหมาย ประวัติโรคติดต่อทางเพศสัมพันธ์ สูบบุหรี่ ประวัติโรคเยื่อบุโพรงมดลูกเจริญผิดที่ ประวัติการ ตั้งครรภ์นอกมดลูกในครรภ์ก่อน และประวัติการมีบุตรร้ายก

ผลการศึกษา : จากการวิเคราะห์ข้อมูลโดย multivariate analysis พบว่าปัจจัยเสี่ยงที่มีความสำคัญต่อการเกิดการตั้งครรภ์นอกมดลูก (OR = จำนวนคุณอน  $\geq 2$ , 3.2, 95% CI (1.75-5.23), มีการคลอดทางช่องคลอดมาก่อน (OR = 0.005, 95% CI (0.002-0.015)), ประวัติการอักเสบในอุ้งเชิงกราน (OR = 3.17, 95% CI (1.40-7.19)), สูบบุหรี่ (OR = 2.49, 95% CI (1.36-4.58)) และการมีบุตรร้ายก (OR = 2.74, 95% CI (1.35-5.54))

สรุปผลการศึกษา : ปัจจัยเสี่ยงการมีคุณอนหล่ายคน โรคติดต่อทางเพศสัมพันธ์ สูบบุหรี่และการมีบุตรร้ายก เป็นปัจจัยเสี่ยงที่สำคัญของการตั้งครรภ์นอกมดลูกในสตรีไทย

คำสำคัญ : ปัจจัยเสี่ยง, การตั้งครรภ์นอกมดลูก

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