

Ectopic Pregnancy and its Risk Factors: A Case Control Study in Nepalese Women

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Abstract

Introduction: Ectopic pregnancy is a significant cause of maternal mortality and morbidity during the first trimester. The major risk factors for ectopic pregnancy include prior tubal infections, previous ectopic pregnancy, previous abortions, use of intrauterine contraceptive devices, contraception failure, tubal surgeries, infertility and use of artificial reproductive pregnancies. This study was carried out to evaluate the effect of different risk factors in the causation of ectopic pregnancies among women in the Nepalese setting.

Materials and methods: This was a case-control study conducted at Kathmandu Medical College comparing 39 cases of ectopic pregnancies with 39 controls consisting of intra-uterine pregnancies. The suspected cases were confirmed through clinical examination, trans-abdominal or trans-vaginal ultrasonography and serum β -hCG levels with further confirmation obtained after laparotomy / laparoscopy among cases who underwent surgery. The two study groups matched with age, gravidity and contraceptive uses were studied. History of previous abortions, previous ectopics and past abdomino-pelvic surgeries were also studied.

Results: There was statistically significant difference in the incidence of contraceptive failure among the two groups (p -value= 0.032) with women with such history having a relative risk of 1.667 with odds ratio of 3.400. The risk posed by previous abortions and previous ectopics wasn't found significant (RR= 1.000 and 2.053 respectively). The history of past abdomino-pelvic surgeries also showed significant role in causation of ectopics (RR= 1.094).

Conclusion: Among different risk factors studied, the contraception usage was the most significant risk factors. Oral contraceptive pills was the most identified among the contraception used in cases of ectopic pregnancy.

Keywords: Ectopic pregnancy.

Introduction

Ectopic pregnancy refers to the implantation of the blastocyst elsewhere than the endometrial lining of the uterine cavity and accounts for 1 to 2 percent of all pregnancies and 6 percent of all pregnancy-related deaths.¹ Apart from being an important cause of maternal mortality during the first trimester, it is associated with a reduction in the subsequent fertility rates and increased risk

of subsequent ectopic pregnancies.² The incidence of ectopic pregnancy is now increasing worldwide with an improvement in the diagnostic techniques. The risk factors for ectopic pregnancy include congenital tubal anomalies, prior tubal infections or sexually transmitted diseases, tubal surgeries, previous ectopic pregnancy, infertility and artificial reproductive technique and failure of contraceptive methods.^{1,3-5} Various contraceptive methods like Oral contraceptive pills, intra uterine contraceptive devices, condoms, I-pills, withdrawal methods, tubal sterilization are frequently practiced in Nepal.

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These methods of contraception may protect from unwanted pregnancy, but their failure may result in ectopic pregnancy. Studies that highlights the role of different risk factors in ectopic pregnancy with the bulk of cases of such pregnancies to be a result of pelvic inflammatory diseases and abortions has been studied.^{6,7} But the risk of ectopic pregnancy and contraceptive practices has not yet been studied clearly in context of Nepal. We, hereby, designed this case-control study with the aim of determining the contraceptive practices in cases of ectopic pregnancy among Nepalese women.

Materials and Methods

This was a case-control study performed at the Department of Obstetrics and Gynecology, Kathmandu Medical College, Kathmandu during a one-year period (1st Feb 2016 to 31st Jan 2017). A total of 39 cases of ectopic pregnancies presented during the study period was compared with 39 intrauterine pregnancies that constituted the controls. Women presenting with relevant history, including amenorrhea, abdominal pain with or without per-vaginal bleeding or spotting were taken as suspects and were diagnosed either through clinical examination, trans-abdominal or transvaginal ultrasonography or serial β -human chorionic gonadotropin (β -hCG) levels or during laproscopic surgery. Relevant clinical findings included abdominal tenderness, palpation of the mass or tenderness in vaginal fornices, cervical motion tenderness. Confirmation was done after laparotomy or laparoscopy except in cases who underwent medical management. Cases of

ectopic pregnancy were enrolled in the study from inpatient ward and controls were enrolled from either outpatient department or inpatient. Control were patients of intrauterine pregnancy taken in after ectopic pregnancy. The controls were also confirmed through trans-abdominal ultrasonography or clinical findings.

The study and control groups were matched demographically in terms of age and gravidity. Questionnaires containing details about the patient regarding smoking status, history of pelvic infections, subfertility, use of ovulation-inducing drugs, tubal sterilization or other tubal surgeries, use of artificial reproductive technology, past abdomino-pelvic surgeries and current contraceptive use were collected and compared between the study and the control groups.

Statistical analysis:

Statistical evaluation of the differences in the study groups was performed using SPSS v 20.0. Z-test for proportion was used to compare proportions of occurrence of risk factors among the study groups while relative risks and odds ratios were used to evaluate the role of a risk factor in the causation of ectopic pregnancy. P-value < 0.05 was taken as significant.

Results

During the study, a total of 39 cases of ectopic pregnancies were compared against 39 cases of normal intrauterine pregnancies. The two groups had no statistically significant difference in terms of age and gravidity as shown in table 1.

Table 1: Demographic characteristics of the study groups

Characteristics of the study group	Study group		P-value
	Cases (Mean \pm SD)	Controls (Mean \pm SD)	
Age	27.56 \pm 4.376	26.67 \pm 4.792	0.391
Gravidity	2.26 \pm 1.464	1.77 \pm 0.842	0.076

Comparison of history of previous abortion among the cases and controls showed identical proportions (p-value= 1.000) in the two study groups, thereby yielding a value of 1.000 to relative risk (95% CI, 0.611- 1.637) and odds ratio (95% CI, 0.371- 2.681).

Thirteen women in the ectopic cases group (33.3%) had contraceptive failure of different sorts. Among them, 8 used oral contraceptive pills, 3 used emergency contraception, 1 used DMPA and 1 had Intrauterine contraceptive device in situ. Five women in the control group (12.8%) had such

accidental pregnancies despite contraceptive usage among whom 4 used oral contraceptives and 1 used DMPA. The difference was significant statistically (p-value= 0.032) with women with contraceptive failure having a relative risk of 1.667 (95% CI, 1.109- 2.506) and odds ratio of 3.4000 (95% CI, 1.075- 10.752).

Table 2: Contraceptive practices in ectopic pregnancy

Contraception	Cases	Control
OCP	8	4
Emergency pills	3	-
DMPA	1	1
IUCD	1	-
Total	13	5

Two patients (5.1%) among the ectopic cases had previous history of ectopic pregnancy while none among controls had such occurrence. The difference was statistically insignificant (p-value= 0.152) with a relative risk of 2.053 (95% CI, 1.631- 2.591) for ectopic pregnancy among women with such history.

Proportions of women in the cases and control groups with history of abdomino-pelvic surgery were closely similar (p-value= 0.761) with 7 (17.9%) and 6 (15.4%) ladies in the two groups respectively. The relative risk was a modest 1.094 (95% CI, 0.624- 1.916) with odds ratio 1.203 (95% CI, 0.365- 3.968).

Table 3: Comparison of risk factors for ectopic pregnancy among the two groups

Risk factor		Study group		χ^2	P-value	Relative risk* (95% C.I.)
		Cases	Controls			
Previous abortion	Yes	11 (28.2%)	11 (28.2%)	0.000	1.000	1.000 (0.611-1.637)
	No	28 (71.8%)	28 (71.8%)			
Previous ectopic	Yes	2 (5.1%)	0 (0.0%)	2.053	0.152	2.053 (1.631-2.591)
	No	37 (94.9%)	39 (100.0%)			
Previous A-P surgery	Yes	7 (17.9%)	6 (15.4%)	0.092	0.761	1.094 (0.624-1.916)
	No	32 (82.1%)	33 (85.6%)			
Contraceptive failure	Yes	13 (33.3%)	5 (12.8%)	4.622	0.032 ^ψ	1.667 (1.075-10.752)
	No	26 (66.7%)	34 (87.2%)			

* Relative risk for ectopic when risk factor is present

^ψ Significant relation between the risk factor and ectopic (p< 0.05)

Discussion

In the current study, no significant difference in the age distribution among the cases and controls was detected. No rise in the incidence of ectopic pregnancy with increasing age was observed. The evaluation of age as a risk factor for ectopic pregnancy in different studies has provided conflicting results.^{4,8-11} A study by

Karaer et al (2006) found that the risk of ectopic pregnancy increased progressively with increasing maternal age, but the association disappeared after 40 years and after adjustment for main risk factors.¹¹ Simms et al (1997) found the incidence of ectopic pregnancy in women aged 40 years or above to be 14 times that observed among those under 16 years.¹² Another

study by Bouyer et al also identified that age was associated per se with a risk of ectopic pregnancy.⁴ Exclusion of cases of ectopic pregnancies with infectious history could be a significant cause of our finding of no association between age and ectopics as most studies with contrasting results attribute such association to the cumulative effects of infectious pathology with increasing maternal age. Additionally, similarity in the ages of the two groups allowed the exclusion of the effect of cumulative risk factors that rise with increasing age of participants.

The proportion of ladies among cases with current contraceptive failure was higher than that among controls with statistically significant difference demonstrated. One third (33.3%) of cases became pregnant despite the use of different contraceptive methods. The proportions showed similarity to those in a study by Basnet et al where the 31.2% of cases with ectopic pregnancy were using temporary methods of family planning.⁹ Most studies highlight increased risk of ectopic pregnancies with intrauterine devices (IUDs).^{6,8,10,11,13-15} Some studies also suggest such risk increases further with increased duration of IUD placement.⁶ Tubal ligation, while proving to be highly effective in preventing intrauterine pregnancies, was found to increase the risk of ectopic in accidental pregnancies in many studies.^{6,8,10,14} The overall incidence of ectopic, though reduced among users of oral contraceptive pills, DMPA and emergency contraceptives as revealed by most studies, the failure of such methods was found to be associated with increased incidence of ectopics.

The incidence of previous abortion among the patients wasn't found to be a significant risk factor for ectopic pregnancy in the current study. Most studies show an increased incidence of ectopic among women with a previous history of abortions^{6,10,11}, however, the results differ in terms of significance of such relation.

Significant association between history of previous ectopic pregnancy and recurrence of such event wasn't established through this study. Most studies highlight such obstetric

history as a significant risk factor for current ectopic pregnancy.^{6,8,11,13} Barnhart *et al* indicated that the risk of facing a repeat ectopic pregnancy increases intensely with the number of prior ectopic pregnancy.¹⁶⁻¹⁸

The absence of significant relation between previous abdomino-pelvic surgeries and ectopic pregnancy was found contrasting to most studies that demonstrate increased risk with surgeries.^{6,8-11,13} It has been reported that previous tubal surgery is a major risk factor for EP with an estimated OR of 4.7 (2.4- 9.5) according to a meta-analysis.¹⁹

Conclusion

Among different risk factors studied, the contraception usage was the most significant risk factors. Oral contraceptive pills was the most identified among the contraception used in cases of ectopic pregnancy.

References

1. Cunningham FG, Leveno KJ, Bloom SL, Spong CY, Dashe JS, Hoffman BL, Casey BM, Sheffield JS. Williams Obstetrics. 24thed. New York. McGraw-Hill Education/ Medical;2004. p 377.
2. Zane SB, Kieke BJ, Kendrick JS, Bruce C. Surveillance in a time of changing health care practices: estimating ectopic pregnancy incidence in the United States. *Matern Child Health J.* 2002;6(4):227-36.
3. Yuk JS, Kim YJ, Hur JY, Shin JH. Association between socioeconomic status and ectopic pregnancy rate in the Republic of Korea. *Int J Gynaecol Obstet.* 2013;122(2):104-7
4. Bouyer J, Coste J, Shojaei T, Pouly JL, Fernandez H, Gerbaud L, et al. Risk factors for ectopic pregnancy: a comprehensive analysis based on a large case-control, population-based study in France. *Am J Epidemiol.* 2003;157(3):185-94.
5. Moini A, Hosseini R, Jahangiri N, Shiva M, Akhoond MR. Risk factors for ectopic pregnancy: a case-control study. *J Res Med Sci.* 2014;19(9):844-9.
6. Li C, Meng C, Zhao W, Lu H, Shi W, Zhang J. Risk factors for ectopic pregnancy in women with planned pregnancy: a case-

- control study. *European Journal of Obstetrics & Gynecology and Reproductive Biology.* 2004; 181:176-82
7. Poonam, Uprety D, Banerjee B. Ectopic pregnancy - Two years review from BPKIHS, Nepal. *Kathmandu University Medical Journal.* 2005;3(12):365-9.
 8. Parashi S, Moukhah S, Ashrafi M. Main risk factors for ectopic pregnancy: a case-control study in a sample of Iranian women. *Int J Fertil Steril.* 2014 Jul-Sep;8(2):147-54.
 9. Basnet R, Pradhan N, Bharati L, Bhattarai N, Basnet BB, Sharma B. To determine the risk factors associated with ectopic pregnancy. *Asian J Pharm Clin Res.* 2015;8(2):93-7.
 10. Khedar S, Mital P, Rajoria L, Gupta D, Shekhawat U, Singhal S. A case-control study to evaluate risk factors for ectopic pregnancy. *Int J Reprod Contracept Obstet Gynecol.* 2016 Aug;5(8):2828-35.
 11. Karaer A, Avsar FA, Batioglu S. Risk factors for ectopic pregnancy: a case-control study. *Aust N Z J Obstet Gynaecol.* 2006 Dec;46(6):521-7.
 12. Simms I, Rogers PA, Nicoll A. The influence of demographic change and cumulative risk of pelvic inflammatory disease on the incidence of ectopic pregnancy. *Epidemiol Infect.* 1997 Aug;119(1):49-52.
 12. Li C, Zhao W, Zhu Q, Cao S, Ping H, Xi X, et al. Risk factors for ectopic pregnancy: a multi-center case control study. *BMC Pregnancy Childbirth.* 2015;15:187.
 13. Li C, Zhao W, Meng C, Ping H, Qin G, Cao S, et al. Contraceptive use and the risk of ectopic pregnancy: a multi-center case-control study. *Eur J Obstet Gynecol Reprod Biol.* 2014;181:176-82.
 14. Pradhan HK, Dangal G, Karki A, Shrestha R, Bhattachan K. Profile of ectopic pregnancy at Kathmandu Model Hospital. *NJOG.* 2015 Jul-Dec;20(2):10-3.
 15. Barnhart KT, Sammel MD, Gracia CR, Chittams J, Hummel AC, Shaunik A. Risk factors for ectopic pregnancy in women with symptomatic first-trimester pregnancies. *Fertil Steril.* 2006;86:36-43.
 16. Chow JM, Yonekura ML, Richwald GA, Greenland S, Sweet RL, Schachter J. The association between Chlamydia trachomatis and ectopic pregnancy. A matched-pair, case-control study. *JAMA.* 1990;263:3164-7.
 17. Skjeldestad FE, Hadgu A, Eriksson N. Epidemiology of repeat ectopic pregnancy: A population-based prospective cohort study. *Obstet Gynecol.* 1998;91:129-35.
 18. Ankum WM, Mol BW, Van der Veen F, Bossuyt PM. Risk factors for ectopic pregnancy: A meta-analysis. *Fertil Steril.* 1996;65:1093-9.