

Risk factors for ectopic pregnancy in a tertiary care hospital

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ABSTRACT

Introduction: Ectopic pregnancy is associated with significant morbidity and mortality. Identifying its risk factors can help in reducing the incidence.

Objective: This study aimed to determine the risk factors for ectopic pregnancy in tertiary care hospital in Nepal.

Methodology: A hospital-based case control study was conducted in Department of Obstetrics and Gynaecology, TU Teaching Hospital, Kathmandu from 14th April 2019 to 12th April 2020. Cases comprised of all the women with ectopic pregnancy undergoing laparotomy or laparoscopy and controls were women delivering on the same day after case enrollment, taken in ratio 1:2. Risk factors were compared and Odds Ratio was calculated. P-value <0.005 was considered significant. Multivariate analysis was done for those risk factors found to be significant from the univariate analysis.

Results: The sample size constituted 75 cases and 150 controls. The incidence of ectopic pregnancy was 1.72% of total deliveries. Mongolian ethnicity (AOR=4.61, 95% CI: 1.94-10.96, p value=0.001) and occupation other than house wife (AOR=2.71, 95% CI: 1.11-6.62, p value=0.028) were found to be associated with ectopic pregnancy. Multigravidity (AOR=4.01, 95% CI: 1.01-15.90, p value=0.048), multiparity (AOR=5.51, 95% CI: 1.03-29.29, p value=0.045), prior history of pelvic inflammation (AOR=20.86, 95% CI: 3.69-117.79, p value=0.001), use of contraceptives (AOR=5.52, 95% CI: 2.19-13.90, p value<0.001) were other factors associated with risk of ectopic pregnancy. Emergency contraceptives use was seen in 28(37.3%) patients.

Conclusion: Mongolian ethnicity, occupation other than house wife, increasing gravidity and parity, pelvic inflammation and emergency contraceptive pills were associated with ectopic pregnancy.

Keywords: Contraception; Ectopic pregnancy; Risk factors.

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INTRODUCTION

Ectopic pregnancy (EP) is one of the most common gynecological emergencies. The incidence of EP has been reported to be 1.3-2.4% of all pregnancies.¹⁻³ resulting in increased maternal morbidity and mortality. It accounts for 1.3-2.4% of all pregnancies. Previously, though laparoscopy was considered as the gold standard for diagnosis of ectopic pregnancy, due to availability of high resolution ultrasound, it has become the first line investigation for the diagnosis of ectopic pregnancy. Methods: It is a prospective study conducted in Manipal Teaching Hospital, Pokhara, from January 2015 till December 2017. All the cases diagnosed with ectopic pregnancy were included in the study. Ultrasonological and intraoperative findings were recorded. Data was analyzed using SPSS (VERSION 16) It is the leading cause of maternal death during the first trimester accounting for approximately 6-10% of all pregnancy-related deaths.⁴⁻⁶ The risk of death from EP is 10 times higher than vaginal delivery, and 50 times greater than induced abortion.⁷

A previous history of an EP is reportedly the most significant risk factor for an EP. The recurrence rate is 15% after the primary EP, and 30% after the second.⁸ Damage to the fallopian tubes from pelvic inflammatory disease (PID), previous tubal surgery, previous abdominal surgery like removal of the appendix, intra uterine contraceptive (IUCD) use, intake of progesterone only pill, infertility and in vitro fertilization treatment also increase the risk of ectopic pregnancy.⁹ Minor risk factors include a history of cigarette smoking, age over 35 years, and multiple sexual partners. However, there was no clear association between ectopic pregnancy and the use of oral contraceptives, previous elective pregnancy termination, miscarriage, or cesarean section.^{10,11}

We conducted this study to determine the socio-demographic, gynaecological, obstetrical, surgical and contraceptive risk factors for ectopic pregnancy.

METHODOLOGY

A hospital- based case control study was carried out in Department of Obstetrics and Gynaecology, Institute of Medicine, Tribhuvan University Teaching Hospital (TUTH), Maharajgunj, Kathmandu, Nepal, from 14th April 2019 AD to 12th April 2020 AD. All cases of ectopic pregnancy, later confirmed by histopathologic examination (HPE) undergoing laparotomy/laparoscopy during the study period were taken as study population and the controls were patient who had delivered, irrespective of the mode of delivery (vaginally or by caesarean section) after 28 weeks period of gestation in the labour room of TUTH within 24 hours after the case enrollment. To improve the statistical significance of the result, two controls were taken for each case of ectopic pregnancy.

A purposive sampling technique was used for the study. Sample size was calculated by using Kelsey's Method, $n = \frac{z^2 \cdot p \cdot (1-p) \cdot (r+1)}{r \cdot (p_0 - p_1)^2}$, where α is probability of type I error (0.05), β is probability of type II error (0.90), P_0 is proportion for cases (Between 0.0 and 1.0), P_1 is proportion for controls (0.751), r is ratio of case-control (2). The calculated sample size was 66 cases. Adding 10% non-response rate required sample size for cases was 71. During study period there were eighty-eight cases of ectopic pregnancy, out of which 75 cases met the inclusion criteria for enrollment as cases. Hence 75 patients were enrolled as cases. Controls were enrolled in the ratio of 1:2, so 150 women, who had delivered after 28 weeks of gestation within 24 hours of case enrollment, were taken as control. Ethical clearance for the study was taken from the Institutional Review Board of Institute of Medicine (IOM), TUTH (IRC no-423/ (6-11) E²/075/76). Only those women who consented to

participate were included in the study after obtaining the written informed consent. Confidentiality of all the information was maintained.

All the patients who fulfilled the inclusion criteria were included in the study. Collection of the data was done through an interview once the patient was comfortable and out of pain. A preformed questionnaire was used. As it is routine to send suspected specimen for HPE, HPE reports of all the case were followed and only the cases with HPE confirmed EP were taken. Control group was taken from labour room who had delivered in labour room of TUTH irrespective of mode of delivery after 28 weeks gestation within 24 hours of case enrollment. Study variables included age, ethnicity, marital status, occupation, gravidity, parity, prior history of spontaneous abortion or induced abortion, prior ectopic pregnancy, prior pelvic infection (history of vaginal discharge, pruritus vulvae, lower abdominal pain, dysuria), prior artificial reproductive techniques, ovulation induction, intrauterine insemination, prior tubal surgery, abdomino-pelvic surgery, recent use of temporary and permanent method of contraceptives (within 1 year of the presentation with EP).

Data analysis was done using IBM SPSS Statistics for Windows, version 25 (IBM Corp., Armonk, N.Y., USA). Crude odds ratio (COR) and 95 % confidence interval for ectopic pregnancy was calculated for all the possible risk factors. Crude OR was adjusted by taking into account of possible influence on other variables, with the use of multiple logistic regression analysis to obtain adjusted OR (AOR), p - value of <0.05 was taken as statistically significance. The COR were adjusted for age, marital status, occupation, gravidity, parity, spontaneous/ induced abortion, contraceptive use, history of infection/ PID, prior ectopic pregnancy, prior abdominopelvic surgery.

RESULTS

During the study period, the total number of deliveries in the hospital were 4932. There were eighty-eight cases of ectopic pregnancy, out of which ten patients were managed medically and 78 patients underwent surgical management and HPE confirmation of ectopic pregnancy was made in 75 patients. Hence 75 patients were enrolled as case. A total of 150 women, who had delivered after 28 weeks gestation within 24 hours of case enrollment, were taken as control.

The incidence of ectopic pregnancy in TUTH during the study period was 1.72% of total deliveries. Among 75 case, 42 (56%) patients had ectopic pregnancy on the

right side. The most common site of ectopic pregnancy was ampullary region of fallopian tube in 54(72%) patients, followed by isthmus region in 14 (18.7%) patients, cornua in 3 (4%) patients, ovary in 2 (2.6%) patients and interstitium in 2 (2.6%) patients. A total of 47 (62.7%) patients had a ruptured ectopic pregnancy, 15 (20%) were tubal abortion and 13 (17.3%) presented as unruptured/organized ectopic pregnancy.

Among cases, 39 (52%) participants were in the 30-39 years age group, whereas 106 (70.6%) participants in control were in the 20-29 years age group. With the increase in the age of women there was increased incidence of ectopic pregnancy. Women of age above 25 years had almost two times higher odds (COR = 1.99, 95% CI: 1.10-3.61) of ectopic pregnancy compared to women below 25 years of age.

Regarding the distribution of ethnicity, case had 38(50.7%) Indo-Aryans and 37(49.3%) Mongolian patients. In the control group there were 112(74.7%) Indo-Aryans and 38(25.3%) Mongolian participants. Mongolian had almost 3 times higher odds (COR=2.86, 95% CI: 1.60-5.14) of ectopic pregnancy compared to Indo-Aryan ethnicity. Mongolians were more likely to have ectopic pregnancy compared to Indo-Aryans. 84 % of the participants were married in case where as all the participants in control groups were married. Among cases, 16% of women were unmarried, divorced and widow. The risk of ectopic pregnancy was high among unmarried and divorced women as compared to married women and the result was statistically significant(p-value = 0.011). Cases included forty-eight housewives, ten

students, ten service-holders and seven local business owners. Other occupation had almost double risk (COR-1.84, 95% CI:1.00-3.38, p-value:0.046) for ectopic pregnancy compared to housewife. This association was statistically significant.

Various obstetric and gynaecological parameters between the cases and control were compared. Multigravida women had 4 times higher odds of ectopic pregnancy compared to primigravida. Pelvic inflammatory disease (PID) and previous abortion were found to be associated with ectopic pregnancy. Prior abdominopelvic surgeries had no significant association with ectopic pregnancy. Other surgeries included appendectomy in two patients, cystectomy in two patients and ovarian reconstruction in one patient. There was no case of tubal reconstructive surgery and three cases had previous EP with unilateral salpingectomy. There was no association of ectopic pregnancy with spontaneous abortion, prior abdomino pelvic surgery, previous history of sub fertility, prior ectopic pregnancy, use of ovulation induction drugs and prior tubal pathology. (Table 1).

Among various methods of contraceptives used by cases, emergency contraceptive pills were highest in number 28(37.3%), followed by Injection Depot Provera users 11(14.7%) (Table 2).

The association of various obstetrical, gynaecological, surgical and contraceptive characteristics were checked by univariate and multivariate logistic regression model with Odds Ratio at 95% confidence interval and p value (Table 3).

Table 1: Comparison of obstetric and gynaecological characteristics between case and control

Variables	Total (N=225) n(%)	Control (N=150) n(%)	Case (N=75) n(%)	OR	95% CI	p-value
Gravidity						
Primigravida	80(35.5)	68 (45.3)	12 (16)	Ref		
Multigravida	145(64.5)	82 (54.6)	63 (84)	4.35	2.17-8.73	<0.001
Parity						
Nullipara	117 (52)	91 (60.6)	26 (34.6)	Ref		
Primipara	82 (36.4)	55 (36.6)	27 (36)	1.71	0.91-3.23	0.094
Multipara	26 (11.5)	4 (2.6)	22 (29.3)	19.25	6.08-60.85	<0.001
Abortion						
Yes	70 (31.1)	33 (22)	37 (49.3)	3.45	1.90-6.25	<0.001
No	155(68.9)	117 (78)	38 (50.7)	Ref		
Spontaneous						
Yes	30 (13.3)	18 (12)	12 (16)	1.39	0.63-3.07	0.407
No	195(86.6)	132 (88)	63 (84)	Ref		
Induced						
Yes	42 (18.6)	15 (10)	27 (36)	5.06	2.48-10.31	<0.001
No	183(81.4)	135 (90)	48 (64)	Ref		

Medical Abortion						
Yes	20 (8.8)	7 (4.6)	13 (17.3)	4.28	1.63-11.25	0.003
No	205(91.1)	143 (95.4)	62 (82.7)	Ref		
Manual Vacuum Aspiration						
Yes	29 (12.8)	9 (6)	20 (26.6)	5.69	2.44-13.27	<0.001
No	196(87.2)	141 (94)	55 (73.4)	Ref		
History of Subfertility						
Yes	7 (3.1)	2 (1.3)	5 (6.7)	Ref	0.03-0.99	0.050
No	218(96.9)	148 (98.7)	70 (93.3)	0.18		
Previous ectopic						
Yes	6 (2.6)	3 (2)	3 (4)	2.04	0.40-10.36	0.389
No	219(97.3)	147 (98)	72 (96)	Ref		
Ovulation induction drugs						
Yes	1 (0.4)	0	1 (1.3)			0.333
No	224(99.6)	150 (100)	74 (98.7)			
Tubal pathology						
Yes	3(1.3)	2 (1.3)	1(1.3)	1.65	0.85-3.20	0.134
No	222 (98.7)	148(98.7)	74 (98.7)	Ref		

Ref: Reference category

Table 2: Comparison of contraceptive use as risk factor between case and control

Contraceptive	Total (n=225) n (%)	Control (n=150) n (%)	Case (n=75) n (%)
None	163 (72.4)	135 (90)	28 (37.3)
Emergency Pill	29 (12.9)	1 (0.7)	28 (37.3)
Oral Contraceptive			
Pills	10 (4.4)	5 (3.3)	5 (6.7)
Depot Provera	19 (8.4)	8 (5.3)	11 (14.7)
Intrauterine			
Contraceptive Device	2 (0.9)	0	2 (2.7)
Implant	1 (0.4)	1 (0.7)	0
Bilateral tubal ligation	1 (0.4)	0	1 (1.3)

Table 3: Univariate and Multivariable logistic regression model for risk factor of ectopic pregnancy

Variables	Univariate analysis		Multivariate analysis	
	Crude OR (95%CI)	p-value	Adjusted OR (95% CI)	p-value
Age (years)				
≤25 years	Ref		Ref	
>25 years	1.99 (1.10-3.61)	0.022	0.58 (0.22-1.51)	0.270
Ethnicity				
Indo-Aryans	Ref		Ref	
Mongolian	2.86 (1.60-5.14)	<0.001	4.61 (1.94-10.96)	0.001
Occupation				
Housewife	Ref		Ref	
Others	1.84 (1.00-3.38)	0.046	2.71 (1.11-6.62)	0.028
Gravidity				
Primigravida	Ref		Ref	
Multigravida	4.35 (2.17-8.73)	<0.001	4.01 (1.01-15.90)	0.048

Parity				
Nullipara	Ref		Ref	
Primipara	1.71 (0.91-3.23)	0.094	0.78 (0.25-2.39)	0.094
Multipara	19.25 (6.08-60.85)	<0.001	5.51 (1.03-29.29)	0.045
Pelvic Inflammatory Disease				
Yes	37 (8.46-161.81)	<0.001	20.86 (3.69-117.79)	0.001
No	Ref		Ref	
Abortion				
Yes	3.45 (1.90-6.25)	<0.001	0.48 (0.13-1.83)	0.290
No	Ref		Ref	
Spontaneous Abortion				
Yes	1.39 (0.63-3.07)	0.407		
No	Ref			
Induced Abortion				
Yes	5.06 (2.48-10.31)	<0.001	0.26 (0.01-5.93)	0.405
No	Ref		Ref	
Medical Abortion				
Yes	4.28 (1.63-11.25)	0.003	6.49 (0.30-140.45)	0.233
No	Ref		Ref	
Manual Vacuum Aspiration				
Yes	5.69 (2.44-13.27)	<0.001	16.67 (0.96-287.65)	0.053
No	Ref		Ref	
Surgery				
Yes	1.65 (0.85-3.20)	0.134		
No	Ref			
Subfertility				
Yes	Ref			
No	0.18 (0.03-0.99)	0.050		
Previous ectopic				
Yes	2.04 (0.40-10.36)	0.389		
No	Ref			
Contraceptive use				
Yes	15.10 (7.43-30.71)	<0.001	5.52 (2.19-13.90)	<0.001
No	Ref		Ref	

Ref: Reference category

DISCUSSION

In our study, 75 women diagnosed as having ectopic pregnancy on laparotomy constituted the cases and for each case, two controls were taken who delivered either vaginally or by caesarean section. The incidence of ectopic pregnancy in TUTH during the study period was 1.72% of total deliveries which is similar to the study done by Mikolajczyk et al (1.3-2.4%).³ In a study from Kathmandu Model Hospital from January 2008 to September 2015, 61 cases of ectopic pregnancy with incidence of 1.46% of total births were reported.¹² The incidence in this study is almost double than that in a study carried out in the department of Obstetrics and Gynaecology, B.P Koirala Institute of Health Sciences, Dharan which found an incidence of ectopic pregnancy

to be 0.93% of total births.¹³ B.P Koirala Institute of Health Sciences, Dharan (Nepal

In univariate regression analysis, various socio-demographic characteristics were seen to be positively associated with ectopic pregnancy. In this study, the majority of the cases were in the age group 30-39 years (52%). Age above 25 years of age had almost two times higher odds (COR=1.99, 95% CI: 1.10-3.61; p value of 0.022) of ectopic pregnancy compared to women below 25 years of age however it was not statistically significant in multivariate analysis at p value of 0.270. This is similar to the study done in other parts of the country which showed the mean age of the patient was 30.1 years with range of 23-45 years in a study conducted at Nepal Medical College Teaching Hospital¹⁴ and age group

of 30-34 years in a study conducted in Department of Obstetrics and Gynaecology, TUTH and Paropakar Maternity and Women's Hospital.⁸

Occupation other than housewife had 1.86 times higher odds of ectopic pregnancy (95% CI: 1.00-3.38, p value of 0.046) compared to housewife in our study. In contrast, study by Basnet et al., showed most of the women were housewife (40.3%) by occupation.⁸ Similarly no significant association was found between ectopic pregnancy and occupation in the studies conducted by Wang et al.¹⁵ Two pregnancies and three or more pregnancies were increased the risk of EP, adjusted odds ratio AOR = 14.39, 95% CI: 2.37, 87.49 and AOR = 14.87, 95% CI: 2.27, 97.38 respectively. The risk of EP in women of previous abdominal or pelvic surgery was also significantly increased (AOR = 4.43, 95% CI: 1.04, 18.92).

This study showed unmarried/separated/widow (16%) were more likely to have ectopic pregnancy and this association was statistically significant. This is higher than the results of the study conducted by Poonam et al.,¹³ which concluded 6.6% were unmarried and lower than Ugbona et al.,¹⁶ in Nigeria between 2011-2013 which showed unmarried women constitutes 46% of cases of ectopic pregnancy.

In our study, Multigravida had 4 times higher odds of ectopic pregnancy as compared to primigravida (COR=4.35, 95% CI: 2.17-8.73, p value<0.001). Multipara had significantly higher risk of ectopic pregnancy compared to primiparous and nulliparous women (COR=19.25, 95% CI: 6.08-60.85). This is consistent with the study by Basnet et al.⁸ In contrast to the present study, the population of nulliparous women was quite high in the study by Poonam et al.¹³ B.P Koirala Institute of Health Sciences, Dharan (Nepal).

Previous history of induced abortion (both MA and MVA) had 4-5-fold [MA (COR=4.28, 95% CI: 1.63-11.25), MVA (COR=5.69, 95% CI: 2.44-13.27)] risk of ectopic pregnancy compared to those without history of abortions however this association was not statistically significant in multivariate analysis at p value of 0.405. This is consistent with the result of the study conducted by Poonam et al., which showed induced abortion was the major risk factor (38.6%).¹³ B.P Koirala Institute of Health Sciences, Dharan (Nepal). A study by Anorlu et al., showed induced abortion increased the risk of ectopic pregnancy by 14 fold.¹⁷

Previous history of PID was significantly associated with higher risk (COR=37; 95% CI: 8.46-161.81) of ectopic pregnancy. Similar with the result of the study conducted

by Poonam et al., pelvic inflammatory disease was the major risk factor for ectopic pregnancy constituting 61.3%¹³ and in study by Basnet et al.,⁸ 18.2% of cases of ectopic pregnancy had history suggestive of ectopic pregnancy. Contraceptive users had significantly higher odds (COR=15.10; 95% CI: 7.43-30.71, p value<0.001) of ectopic pregnancy compared to non-user. Similar to the result of the study conducted by Bhandari et al., which showed oral contraceptive pills was the most identified among the contraception used in cases of ectopic pregnancy.¹⁸

There was no association of ectopic pregnancy with marital status, spontaneous abortion, prior abdomino pelvic surgery, previous history of sub fertility, prior ectopic pregnancy, use of ovulation induction drugs, prior tubal pathology in univariate analysis. In contrast to the present study, the study by Muzaffar et al., (2018-2020) had higher risk with 12.7% of cases of EP with prior ectopic pregnancy with an OR of 8.129.⁷ A study by Pradhan et al., reported the incidence of recurrent EP of 16.7%¹⁴. The study by Parashi et al., showed that there was a strong correlation between abdominopelvic surgery and risk of extrauterine pregnancy. Prior abdominopelvic surgery was associated with an increased risk of EP (AOR=5.24, 95% CI: 2.04-13.4).¹⁹ Similarly the study by Belquis et al., reported 20.8% of cases of EP had a history of abdominopelvic surgery.²⁰

In multivariable logistic regression model, Mongolian ethnicity compared to Indo-Aryan ethnic group had 4.6 times higher risk of developing ectopic pregnancy (AOR=4.61, 95% CI: 1.94-10.96). Housewife had lower risk of ectopic pregnancy where as other occupation had almost 3 times risk of ectopic pregnancy (AOR=2.71, 95% CI: 1.11-6.62). Multigravida compared to primigravida had 4 times higher risk of ectopic pregnancy (AOR=4.01, 95% CI: 1.01-15.90). Multipara compared to primiparous or nulliparous had 5.51 times higher odds of ectopic pregnancy (AOR=5.51, 95% CI: 1.03-29.29). Contraceptive users compared to non-users had 5.5 times greater risk of developing ectopic pregnancy (AOR=5.52, 95% CI: 2.19-13.90). Women with previous history of PID were more likely to have ectopic pregnancy compared to those without history of PID (AOR=20.86, 95% CI: 3.69-117.79).

The limitation of this study was that this was a single hospital-based case control study and the study sample would not be representative of the general population. The sample size was small and a larger sample size would be clearly indicated to draw more valid inferences to a large population to adequately assess the risk factors associated with ectopic pregnancy.

CONCLUSION

Sociodemographic factors of a woman like Mongolian ethnicity and occupation other than house wife showed significant association with ectopic pregnancy. Other than this increasing gravidity and parity, history of PID

are also significantly associated with ectopic pregnancy. Use of contraceptives methods has increased risk of ectopic pregnancy. The use of emergency contraceptive pills showed the higher risk of ectopic pregnancy.

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