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Research Article

TO DETERMINE THE RISK FACTORS ASSOCIATED WITH ECTOPIC PREGNANCY

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ABSTRACT

Objective: To determine the risk factors associated with ectopic pregnancy (EP).

Methods: A descriptive study was carried out in Department of Obstetrics and Gynecology, Tribhuvan University Teaching Hospital (TUTH) and Paropakar Maternity and Women's Hospital (PMWH) from May to November 2013. Women diagnosed and operated for EP were interviewed using semi-structured questionnaire after second post-operative day.

Results: Among 77 cases (44 from PMWH and 33 from TUTH) of EP out of 13,424 total deliveries during the study period (0.5%), the frequency of EP was 1 in 79 deliveries in TUTH and 1 in 245 deliveries in PMWH. The most common presenting symptom was abdominal pain. The peak age group was 30-34 years (n=21). Most of them were multipara 30 (39%) and 61% had first pregnancy between age group of 19 and 24 years and 33.8% of women had home delivery. 33% of the women gave history of abortion and among them almost equal number of women had spontaneous abortion (n=17) or induced abortion (n=16). History suggestive of PID was found in 14 women. History of emergency contraceptive taken within 45 days of presentation was present in 18 women. Majority of patients had taken emergency contraceptive before 29-30 days. History of current use of oral contraceptive was present in 4, depo-provera in 7 and cupper-T in 6 patients.

Conclusion: Abdominal pain was the single most common clinical presentation of EP. The most identified risk factors were abortions and emergency contraceptive, followed by PID, infertility, depo-provera, intra uterine contraceptive device, and previous EP.

Keywords: Ectopic pregnancy, Risk factor, Prevalence, Emergency contraceptive, Temporary family planning.

BACKGROUND

Ectopic pregnancy (EP) is one of the commonest acute abdominal emergencies a gynecologist has to meet in his day-to-day practice. It refers to the implantation of a fertilized egg in a location outside of the uterine cavity, including the fallopian tubes (approximately 97.7%), cervix, ovary, cornual region of the uterus, and abdominal cavity. For tubal pregnancies, the ampulla is the most common site of implantation (80%), followed by the isthmus (12%), fimbria (5%) and others (3%) [1]. EP was first described in the 11th century and until the middle of the 18th century it was usually fatal. Approximately, 2% of pregnancies are ectopic [2]. EP is the leading cause of maternal mortality in Africa accounting 0.5% of all maternal deaths, and also in Asia where it accounts for 0.1% of maternal deaths [3]. By 1992, the number of ectopic pregnancies has increased to 108,800. Concurrently, however, case fatality rate decreased from 35.5 deaths per 10,000 cases in 1970 to 2.6 per 10,000 cases in 1992 indicating it as major health problem to cause mortality in the world [4].

Most ectopic pregnancies occur when a fertilized egg attaches to the inside lining of a fallopian tube (a tubal EP). If not treated quickly enough, the tube can burst, causing internal bleeding, which can lead to collapse and even death. EP can be difficult to diagnose because symptoms often mirror those of a normal early pregnancy [1]. There are several risk factor associated with EP. The greatest risk factor for an EP is a prior history of an EP. The recurrence rate is 15% after the first EP, and 30% after the second. Similarly, infection, congenital abnormalities, or tumors of the fallopian tubes can increase a woman's risk of having an EP. Similarly, previous surgery on the fallopian tubes such as tubal sterilization or reconstructive, pelvic infections due to Chlamydia or *Neisseria gonorrhoeae*, pelvic infections, conditions such as endometriosis, fibroid tumors, or pelvic scar tissue (pelvic adhesions) can increase the risk of an EP. Cigarette smoking around the time of conception has also been associated with an increased risk of EP and this risk was observed to be dose-dependent [5]. Presence of the following factors increases the possibility of EP in any sexually active woman of child-bearing age: Such as age between 25 and 34 years old, history of pelvic inflammatory disease, previous abdominal surgery, such as removal of the appendix, intra uterine contraceptive device (IUCD), taking progesterone-only contraceptive pill, infertility and *in vitro* fertilization treatment [1].

Ultrasound is a useful tool in the diagnosis of EP. Both the surgical and the medical management exist for the EP, but the initial management decision is based on the patient's stability and the type of EP. Only a few studies regarding EP were done in the eastern and western Nepal and Kathmandu. This study was carried with the aim to evaluate the clinical presentation, prevalence, most common risk factors associated with EP in Tribhuvan University Teaching Hospital (TUTH) and Paropakar Maternity and Women's Hospital (PMWH) of Thapathali in Kathmandu, Nepal.

METHODS

Design

Hospital-based cross-sectional study was undertaken in the months of May-November 2013 with study period of 7 months.

Study settings

The study was carried out in the Department of Gynecology, TUTH and PMWH of Thapathali in Kathmandu, Nepal. These hospitals provide care at tertiary level. TUTH is one of the largest teaching hospitals, and PMWH is the one of the largest maternity hospital of Nepal.

Study population and sample size

Patients admitted with the diagnosis of EP and treated in the department of gynecology of TUTH and PMWH, Thapathali, Kathmandu were selected for the study. The patients who were diagnosed as EP of any reproductive age at study site were taken as study unit. Purposive sampling method was adopted for sampling. Base sample size of 77 pregnant women who came in the two hospitals during the study period was calculated for study purpose at 95% confidence interval, 0.093 estimated proportion of all EP patients [6] and margin of error at 0.0153.

Analysis

Data entry, data checking, compiling and editing was done manually, and data analysis was done as per the objective of the study. Data analysis was performed in Statistical Package for Social Science software version 18.0 software. The results are projected as proportions and percentages.

Ethical consideration

Ethical clearance was taken from IOM, TUTH, MMC and research committee of PMWH, which is one of the authorized institutions of ethical board of NHRC. Written permission was taken from the Department of Pharmacy and Research Committee of PMWH. Verbal consent was taken from the respondents before the interview. At any point, the respondents were permitted to terminate the interview.

RESULTS

Demographic characteristic

Among 77 cases, most of the women (40.3%) were housewife by occupation. More than one fourth women (27.3%) were involved in service, among them four were teachers. About 87% of the women were Hindu by religion. The ethic group composition of the study population was divided into two groups i.e. Indo-Aryan and Mongolian. Indo-Aryan group consisted Brahmin (19) and Chhetri (19) with only two women of Madhesi origin. Mongolian ethnicity consisted mainly Tamang (17), followed by Magar (9) and Newar (9) and Gurung (2). Most of the women had achieved an intermediate level education (28.6%), followed by secondary level education 16 (23.4%). Majorities (96.1%) were married. Age at marriage was mostly in between 16-20 years (49.4%) and 21-25 years (28.6%) (Table 1).

Table 1: Demographic characteristic of the respondents

Characteristic	Frequency (N=77)	Percent (N=100)
Occupation		
Housewife	31	40.3
Service	21	27.3
Small business	13	16.9
Agriculture	8	10.4
Student	4	5.2
Religion		
Hindu	67	87.0
Buddhist	10	13.0
Ethnic group		
Indo-Aryan	40	52
Mongolian	37	48
Education		
Illiterate	13	16.9
Primary (1-5)	12	15.6
Secondary (6-10)	16	23.4
Intermediate	22	28.6
Higher education	12	15.6
Marital status		
Unmarried	3	3.9
Married	74	96.1
Age at marriage		
10-15	8	10.4
16-20	38	49.4
21-25	21	27.3
26-30	6	7.8
31-35	1	1.3
Mean=20		

Clinical presentation

Of the 77 cases majority of the patient visited the hospital due to abdominal pain (53.2%), followed by abdominal pain and cessation of menses (22.1%) and 18.2% came to hospital due to abdominal pain and bleeding (Table 2).

Age distribution of patients

Table 3 shows age wise distribution of study population. Most of the women belonged to the age group of 30-34 years (27.3%) and 25-29 years (26%).

Obstetric factor

About 61% of woman had their first pregnancy between the age group of 19 and 24 years. Out of 77 EP majority of patients were multipara (39%). Majority of women in the study had home delivery (33.8%). Six of the women gave a history of still birth (Table 4).

Abortion and previous EP

43% of the women in the study gave history of abortion and among them almost equal number of women had spontaneous abortion (n=17) or induced abortion (n=16). Seven of the women gave a history of previous EP (Table 5).

Table 2: Clinical presentation

Cause of hospital visit	Frequency (N=77)	Percent (N=100)
Cessation of menstruation only	1	1.3
Abdominal pain only	41	53.2
Bleeding only	1	1.3
Cessation of menstruation and abdominal pain	17	22.1
Abdominal pain and bleeding	14	18.2
Bleeding and severe vomiting	1	1.3
Burning micturition, abdominal pain and white discharge	2	2.6

Table 3: Age distribution of patient

Age group	Frequency (N=77)	Percent (N=100)
≤19	2	2.6
20-24	17	22.1
25-29	20	26.0
30-34	21	27.3
35-39	16	20.8
≥40	1	1.3
Mean=29	SD=5.5	

SD: Standard deviaton

Table 4: Obstetric factor

Variable	Frequency (N=77)	Percent (N=100)
Age at first pregnancy		
12-18	17	22.1
19-24	47	61.0
25-30	13	16.9
Mean=21		
Parity		
Nulliparous	26	33.8
Primiparous	21	27.3
Multiparous	30	39
Mean parity=1.12		
Mode of delivery		
Home delivery	26	33.8
Hospital delivery	13	16.9
Caesarian section	3	3.9
Both home and hospital delivery	9	11.7
Both hospital delivery and caesarian section	1	1.3
Nullipara	25	32.5

Risk factors of EP

Only two women were found to be a smoker. In the history of PID symptoms, most of the patients had abdominal pain and per vaginal discharge (n=20) and only abdominal pain was present in 17 women and only per vaginal discharge was present in one. History suggestive of PID was taken when all three symptoms, i.e. abdominal pain, vaginal discharge and fever were present, which was found in 14 women. Similarly, other risk factor such as history of infertility was found in 10, pelvic operation in 7 and disease of the genitourinary tract in 2 women, respectively. None of the women gave a history of appendicitis and *in vitro* fertilization. Of 7 pelvic operation, 6 were for ectopic and one for ovarian cyst (Table 6).

Current user of emergency contraception

Current use was considered when the woman presented within 45 days of taking emergency contraception. Among the 77 EP patients, 23.4% of the women had a history of using an emergency contraceptive within 45 days. Maximum patients had taken emergency contraceptive before 22-35 days (Table 7).

Current user of temporary family planning

Women who became pregnant while taking temporary methods of contraceptives were 24 (31.2%). Among them 26% were non-oral user and rest were oral user. Maximum patients were taking it continuously (n=13) rather than intermittently EP was the main reason cause to stop (Table 8).

DISCUSSION

EP continues to be the leading cause of first-trimester maternal death [4]. Since 1970, the frequency of EP has increased six-fold, and it now occurs in 2% of all pregnancies [7].

Table 5: Abortion and previous EP

Variable	Frequency	Percent
Abortion		
Yes	33	42.9
No	44	57.1
Type of abortion		
Spontaneous	17	22.1
Induced	16	20.8
Age at abortion		
16-20	4	5.2
21-25	12	15.6
26-30	11	14.3
31-35	5	6.5
36-40	1	1.3
History of previous EP		
Yes	7	9.3
No	70	90.9

EP: Ectopic pregnancy

Table 6: Risk factors of EP

Risk factor	Frequency (N=77)	Percent (N=100)
History of smoking		
Yes	2	2.6
No	75	97.4
History of PID		
Yes	14	18.2
No	63	81.9
Infertility		
Yes	10	13
No	67	87.1
History of disease related to genitourinary tract		
Yes	2	2.6
No	75	98.7
History of pelvic operation		
Yes	7	9.1
No	70	90.9

EP: Ectopic pregnancy

Prevalence

The frequency of EP in this series was 1.01 of the total delivery (n=33) i.e. 1 in 89 deliveries in TUTH and 0.0040 of the total delivery (n=44) i.e. 1 in 245 delivery in PMWH. The prevalence of EP combined in the two hospitals was 0.5%. The incidence of EP was 1 in 87 deliveries in the study of Sharma *et al.,* (2011) [8] which is close to the number in TUTH but less than the PMWH. The incidence of EP in the study by Poonam *et al.,* (2005) [6] was 0.93 of total births, which are close to TUTH and higher than PMWH. In the study of Aziz *et al.,* (2011) [9] the frequency of EP was 0.58%, which is similar to this study (0.57%). The low prevalence in PMWH could be due to this hospital being well known for maternity care while high prevalence in TUTH could be due to this hospital providing multidisciplinary care service.

Socio-demographic characteristics

In the study of Poonom [6] *et al.,* (2005) the majority of patient 52 (69.3%) had low socioeconomic status. In this study, most of the women were housewife (40.3%) by occupation, 27.3% women were in service, 16.9% in small business and 10.4% in agriculture this could be due to study conducted in Kathmandu. Most of the women in the study were Hindu 67 (87%) followed by Buddhist 10 (13%) as expected as most of the people follow Hindu religion.

Most of patients in this study were of Indo-Aryan ethnicity in contrast to the study by Pradhan *et al.,* (2006) [10], but similar to the study by Sharma *et al*., (2011) [8]. This could be due to the difference in the study population between Central, Western and Midwestern region. In the study of Sharma *et al.,* (2011) [8] incidence of EP was more in Mongolian group.

In the study of Udigwe and Umeononihu (2010) [11] conducted in Nigeria 28 (77.7%) were married and 20 (55.6%) attained secondary school as their highest level of education. In the study of Poonom *et al.,* (2005) [6] there were 70 (93.3%) married and 5 (6.6%)

Table 7: Current user of emergency contraception

Variable	Frequency	Percent
Current user		
Yes	18	23.4
No	59	76.6
Advised by		
Husband	7	9.1
Medical practitioner	11	14.3
Interval between clinical presentation and intake of emergency contraceptive		
≤7 days	1	1.3
8-14	1	1.3
15-21	2	2.6
22-28	6	7.8
29-35	7	9.1
>35	1	1.3
Emergency contraceptive method		
Econ	8	10.4
i-pill	8	10.4
Could not specify	2	2.6

Table 8: Current user of temporary family planning

Variable	Frequency	Percent
H/O of current user		
Yes	24	31.2
No	53	68.8
Methods		
Oral (combined-Nilocan white)	4	5.2
Non-oral	13	16.9
Non oral methods		
Cupper-T (IUCD)	6	7.8
Depo (sangini)	7	9.1

IUCD: Intra uterine contraceptive device

unmarried women, which was conducted in BPKIHS, Dharan, Nepal. In this study, 96.1% were married, and most of the women had acquired intermediate level (28.6%) of education, followed by secondary level 16 (23.4%). The raised level of education could be due to the women studied being in the capital city. Majority of women were married by the age of 16-20 years (49.4%), followed by the age group of 21-25 years (28.6%). Similarly age of the women when they had their first pregnancy were in between 19 and 24 years in the majority (61%), followed by the age group of 12-18 years (22%). Only 16.9% of the sample population had their first pregnancy in between the age group of 25 and 30 years.

Clinical presentations

The symptoms at presentation: Abdominal pain, amenorrhea, and vaginal bleeding followed the global trend [6,12,13]. In the study by Poonam *et al.,* (2005) [6] the most frequent presenting complaints was (58.6%) amenorrhea of 6-10 weeks. In the study of Shah and Khan, (2005) [14] among the clinical features, the most common presenting symptom was abdominal pain in 37 (97.3%) patients whereas history of amenorrhea and vaginal bleeding were found in 28 (73.6%) and 22 (57.8%) patients respectively which is similar to this study. In this study out of the 77 cases majority of the patient visited the hospital due to abdominal pain 41 (53.2%), likewise 14 (18.2%) came to hospital due to abdominal pain and bleeding and 17 (22.1%) came to hospital due to cessation of menstruation and abdominal pain. In addition, two patients came due to burning micturition, abdominal pain and white discharge while one patient each visited due to bleeding with pain abdomen and bleeding and severe vomiting. The classic clinical trial of EP is pain, amenorrhea, and vaginal bleeding. Unfortunately, Only 50% of patients present typically [6] similar findings were noted in this study.

Age

Mean age was 30±4 years in the study of Aziz *et al.,* (2011) [9] and 30.29±6.084 years in the study of Sharma *et al.,* (2011) [8], which is almost close to this study. In the present study mean age was 29±5.5 and the risk of EP increased progressively with maternal age. More than 50% of the women were in between 25 and 34 years age group and almost half of them 37 (48.1%) were in the age group between 21 and 30 years which is similar to their study. In the other study the peak age group was 26-30 years [6,11-13,] and 25-29 (27%) in Karki *et al.,* (2009) [15]. In the study of Sharma *et al.,* (2011) [8] the majority of cases were in the age group between 31 and 35 years. This is slightly higher than the present study. The increased frequency of EP in this study coincides with the age group of peak sexual activity and reproduction in the Nepalese population.

Parity

In the study by Aziz *et al*., (2011) [9] EP was more common among multipara, which is similar to this study. 39% women were multipara in this study. The population of nulliparous women was also quite high in the present study, which is similar to Poonam *et al.,* (2005) [6]. However in the study done by Sharma *et al.,* (2011) [8] mean parity was 3.1. In a Nigerian study of Gharoro and Igbafe (2002) [16] 49.3% were nulliparous women in contrary to this study. Majority of women in this study had home delivery 26 (33.8%) and only 16.9% women had hospital delivery. Similarly, there were nine women who had both home and hospital delivery. There was only one patient who had a cesarean section in the past.

Risk factors

There are a number of risk factors that lead to tubal damage and dysfunction predisposing to EP while there is overlap, these can be generalized as mechanical and functional factors. Mechanical factors like salpingitis, prior tubal surgery, prior EP, prevents or retard the passage of the fertilized ovum into the uterine cavity. Functional factors like changes in serum level of estrogens and progesterone delay passage of the fertilized ovum into the uterine cavity by altering the tubal motility [17].

Smoking

In the study by Cunninngham *et al.,* (2001) [17] smoking was one of the risk factor for EP as it delays passage of the fertilized ovum into the uterine cavity by altering the tubal motility. This association cannot be correlated as there were only two women who smoked (2.6%) in this study.

Abortion

An induced abortion was the major risk factor and its contribution was 38.6% in Poonam *et al.,* (2005) [6] similarly in the study by Aziz *et al.,* (2011) [9]. 37.8% of the patients had a previous history of either spontaneous or medically induced abortion. History of previous abortion is suggestive of tubal damage due to ascending infection as contributing factor for EP. The finding is also consistent with the study done in Enugu [18], Lagos [19], Benin city [16] and the Niger Delta. In this study 33 (49.2%) patient had a previous abortion and among them almost equal number of women had either spontaneous (n=17) or induced abortion (n=16).

Previous pelvic operation and EP

In the study by Karki *et al.,* (2009) [15] 9 (14%) had a history of previous pelvic operation. In this study 7 (9.1%) women had pelvic operation among them six women had previous tubal surgery. This is found to be lower than the study by Karki *et al.,* (2009) [15]. In this study 7 (9.1%) were previous EP. This is similar to the study of Aziz *et al.,* (2011) [9] and Shah and Khan, (2005) [14] which was 9% and 7.8% respectively.

PID

Six out of 21 patients had pelvic inflammatory disease as the risk factors in the study of Sharma *et al*., (2011) [8]. Other studies from different parts of the world had also shown pelvic inflammatory disease as a significant risk factor [8,10,15,20,21]. In the study by Poonam *et al.,* (2005) [6] conducted in BPKISH, Dharan, Nepal, pelvic inflammatory disease was the major risk factor described and its contribution was 61.3%. In the present study only 18.2% of the women had a history suggestive of PID. History suggestive of PID was taken when all the three symptoms i.e. abdominal pain, vaginal discharge and fever were present. This is similar to Sharma *et al.,* (2011) [8]. There are chances of forgetting when patients are asked to recollect the symptoms they had in the past.

Infertility

In the study by Shah and Khan (2005) [14] and Karki *et al.,* 2009 [15], 9 (23.6%) and 9 (14%) had a history of previous infertility respectively. In this study, 13% women had a history of previous infertility, which is lower than their study. Of 77 cases, none of the women gave the history of appendicitis and *in vitro* fertilization.

Current use of emergency contraceptive

Low-dose daily progestogen-only oral contraceptive pills are effective at preventing pregnancy but if this method fails, pregnancies are more likely to be ectopic than those occurring among users of other contraceptive methods [22]. A possible explanation is that progesterone modifies tubal function, reduces contractility and thus slows the rate of ovum or blastocyst transport. By the same mechanism, ectopic pregnancies might occur following treatment failure with a progestogen-only emergency contraceptive pill [23]. In this study, almost one fourth of cases (23%) had a history of currently using an emergency contraceptive, and all of them had used oral pill (I pill, Econ), which are progesterone containing pill. Most of the patients were advised by medical practitioner to take emergency contraceptive and 17% of them had taken within 35 days.

Current use of temporary family planning

In this study, patients currently using temporary family planning methods were found to be 31.2%, among them 19 (24.7%) were non-oral user and 4 (6.5%) were oral users. Although IUCD user are supposed to be protected from both intra and extra uterine pregnancy, it has been found that a women who conceives with IUCD *in situ* is 7 times

more likely to have tubal pregnancy as compared to a woman who conceives without IUCD [24]. In the study of Karki *et al.,* (2009) [15] and Majhi *et al.,* (2007) [12]. IUCD users were 31% and 6.1% respectively. Similarly in the study of Aziz *et al.,* (2011) [9] conducted in Yanbu, KSA, Kingdom of Saudi Arabia 4.5% of patients were IUCD users. In this study, depo provera and IUCD users were found to be most commonly associated with EP (7.8%). This is similar to Majhi *et al.,* (2007) [12] and higher than the study by Aziz *et al.,* (2011) [9]. In the study by Poonam *et al.,* (2005) [6] 12 (16%) used depo-provera.

The most identified risk factors associated with EP in this study were abortions and emergency contraceptive, followed by PID, infertility, depo-provera and IUCD use and previous EP.

CONCLUSIONS

There were a total of 77 cases of EP out of 13424 total deliveries during the study period, making it 0.5% of total deliveries. The frequency in TUTH was 1 in 79 deliveries and in PMWH were 1 in 245 deliveries. Hindu and Indo-Aryan women were maximum in the study. Most of the women were multipara. Abdominal pain was the single most common clinical presentation of EP. The most identified risk factors were abortions and emergency contraceptive followed by PID, infertility, Depo provera, IUCD, and previous EP. However, risk factors may not always be present. Therefore, EP should be suspected in every woman of reproductive age who presents with unexplained abdominal pain, irrespective of amenorrhea and vaginal bleeding and whether risk factors are present or not.

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