

Ectopic pregnancy

Prevalence and risk factors in women attending a tertiary care hospital in Saudi Arabia

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ABSTRACT

الأهداف: التعرف على مدى انتشار الحمل خارج الرحم، بالإضافة إلى طرق العلاج، وعوامل الخطر المرتبطة بهذا الحمل.

الطريقة: أُجريت هذه الدراسة الاسترجاعية خلال الفترة من يناير 2000م إلى ديسمبر 2010م وذلك على كافة الحالات المصابة بالحمل خارج الرحم واللاتي تم تحويلهن إلى مستشفى الملك فهد الجامعي، الخبر، المملكة العربية السعودية. لقد قمنا بجمع كافة البيانات المتعلقة بكل من: العمر، وعدد مرات الحمل، والولادات السابقة، والتاريخ المرضي للحمل الحالي، واستخدام علاج لتأخر الحمل، والطرق التشخيصية والمعلومات التي وُصل إليها، وتاريخ ونوعية الجراحة.

النتائج: لقد كانت نسبة انتشار الحمل خارج الرحم 1.13%، وكان متوسط عمر المرضى 30.42 ± 6.9 عاماً. ولقد كانت 108 مريضة (41.7%) قد حملن من قبل وذلك بالمقارنة مع 151 مريضة بكر (58.3%) ($p=0.0002$, 95% CI: greater than or equal to -0.0811) ولقد حمل 84 مريضة حملاً تلقائياً بعد الحمل خارج الرحم. وكان متوسط عمر 31 مريضة 28.9 ± 6.9 عاماً، فيما كان متوسط عمر 53 مريضة 39.59 ± 5.9 عاماً. ($p < 0.001$, 95% CI: greater than or equal to -11.8735) ولقد كانت آلام البطن (العدد: 251) والنزيف المهبلي (العدد: 240) من أكثر الأعراض انتشاراً بين المرضى.

خاتمة: أوضحت هذه الدراسة التي استمر تحليلها على مدى 10 سنوات أن نسبة حدوث الحمل خارج الرحم في منطقتنا مشابه لما قد ورد في المراجع العالمية. ولقد كان المرضى الذين عُمل لهم أطفال أنابيب، أو تنشيط المبايض، أو يوجد لديهم تاريخ مرضي بالحمل خارج الرحم هم أكثر عرضة لحدوث هذا الحمل مرة أخرى. وكان العمر من العوامل المهمة المساعدة لحصول الحمل خارج الرحم عند السيدات اللاتي ولدن أطفالاً من قبل.

Objectives: To find the prevalence, risk factors, and pattern of management of ectopic pregnancy (EP).

Methods: This retrospective study was conducted between January 2000 and December 2010 in all patients admitted to King Fahd Hospital of University, Al-Khobar, Kingdom of Saudi Arabia. Patients with suspected history of EP were collected. We collected the following data: age, parity, history of present pregnancy, any infertility treatment, diagnostic methods, and findings.

Results: The prevalence of EP was 1.13%. The average age was 30.42 ± 6.9 years. One hundred and eight (41.7%) women had previous pregnancies compared to 151 (58.3%) ($p=0.0002$, 95% CI of difference: greater than or equal to -0.0811 compared to primigravida. Eighty-four women had spontaneous pregnancy post EP. Thirty-one were 28.9 ± 6.9 and 53 women were of 39.59 ± 5.9 years ($p < 0.001$; 95% CI of difference greater than or equal to -11.8735). Abdominal pain (n=251) and vaginal bleeding (n=240) was the most common presenting symptom.

Conclusion: This 10-year analysis showed that incidence of EP in our region is within the range as reported in the literature. Those who are undergoing in vitro fertilization (IVF), ovulation induction (OI), previous EPs are significantly more prone to acquire EP second time around. Age was an important risk factor for developing EP in women who had borne children.

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Ectopic pregnancy (EP) is a common condition among women of childbearing age and an incidence of 1-3% has been reported in the Western World,^{1,2} and in US annually 1 of 1000 women between 15 and 44 years old are diagnosed with ectopic pregnancy.³ Two small studies from different regions of Saudi Arabia reported an incidence of 0.58-0.74%.^{4,5} Pelvic infections, smoking, previous tubal surgery, genital infections, intra-uterine devices use, and endometriosis have been suggested as risk factors.⁶⁻⁸ Moreover, women who had history of EP are also at increased risk of a repeat ectopic pregnancy.⁹ The most common site of EP is in the fallopian tube and other sites EP have been reported but low incidence.¹⁰ Ruptured EP, which is a life-threatening emergency, is responsible for 10-15% of all maternal deaths.¹¹ It was reported that abdominal pain and vaginal bleeding approximately 7 weeks after amenorrhea is the most common symptoms,¹² but these symptoms could be of patients with miscarriage/abortion; thus, high index of suspicion of EP should be carried in equivocal presentations with immediate ultrasonographic examination. Management of EP varies from observant to radical surgery depending on the duration of the symptoms, presentation to the hospital, and clinical signs of rupture.^{13,14} Patient's selection for medical management is important because it requires close monitoring and follow up.¹⁵ The prevalence of EP in Saudi Arabia is not known as few studies have reported small number of cases. The aim of this study is to find the prevalence of EP, the risk factors, mode of management, and outcome.

Methods. We retrospectively reviewed the clinical records of patients admitted to King Fahd Hospital of the University, Al-Khobar, Kingdom of Saudi Arabia between January 2000 and December 2010 with a suspected history of EP. We collected the data from the hospital registry using the International Classification of Diseases (ICD) (The ICD 9th Revision code 63316 during 2000 and 2010).¹⁶ King Fahd Hospital of the University is the teaching institution of College of Medicine of University of Dammam. The Deanship of Scientific Research, University of Dammam approved the ethical papers of this study.

We collected the following data: age, parity, history of present pregnancy, any infertility treatment, diagnostic

methods, and findings. The date of surgery and histological examination of tissue removed was retrieved. Patients who were proved to be EP were included in the analysis. The prevalence of EP in 10-year age period was calculated by number of registered pregnancies during the study period. The extra uterine ratio is defined as the number of ectopic pregnancies divided by the number of births.¹⁷ The prevalence of first versus repeat EP and the proportion of patients with first EP and prior infertility treatment or intrauterine contraceptive device (IUCD) use at the time of the diagnosis was calculated.

Statistical analysis. Data analysis was performed using SPSS (Statistical Package for the Social Sciences), Version 14.0 (SPSS Inc., Chicago, IL, USA). The results are presented as mean \pm standard deviation (SD). Statistical significance of differences between groups were determined with Student's t-test and p values of 0.05 using confidence interval (CI) of 95% were considered as significant.

Results. There were 259 patients who were admitted with EP during the study period wherein 22969 deliveries were conducted giving an incidence of 1.13%. The average age was 30.42 \pm 6.9 years. One hundred and seventy one (66%) were Saudi nationals and the rest were expatriates. The risk factors for EP are shown in Table 1. One hundred and eight (41.7%) women had previous pregnancies compared to 151 (58.3%) EP was the first pregnancy ($p=0.0002$, 95% CI of difference: greater than or equal to -0.0811). Eighty-four women had spontaneous pregnancy (post EP). Thirty-one were of average age of 28.9 \pm 6.9 and 53 women were of 39.59 \pm 5.9 years ($p<0.001$; 95% CI of difference greater than or equal to -11.8735). Abdominal pain (n=251) and vaginal bleeding (n=240) was the most common presenting symptom. The other symptoms were spotting in 19 (7.3%), vomiting in 16 (6.17%), and hemorrhagic

Table 1 - Risk factors of ectopic pregnancies (N=259).

Risk factors	n	(%)
IUCD	11	(4.2)
Abortions	19	(7.3)
Pregnancy with IVF	24	(9.3)
Pregnancy with OI	23	(8.9)
Cesarian sections	26	(10.0)
Previous ectopic pregnancy	31	(12.0)

IUCD - intrauterine contraceptive device, IVF - in vitro fertilization, IO - ovulation induction

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Table 2 - Post-ectopic pregnancy obstetrics history (N=259).

Obstetrics history	n	(%)
Spontaneous pregnancy	84	(32.4)
No pregnancy	72	(27.7)
Ovulation induction	39	(15.1)
IVF pregnancy	34	(13.1)
Recurrent ectopic	30	(11.6)
IUCD - intrauterine contraceptive device, IVF - in vitro fertilization		

shock in 6 (2.31%). The average gestational age was 6.62 ± 8.4 years. At the time of admission, all patients underwent ultrasound confirmation and 170 (65.6%) had beta HCG ordered. The mean beta HCG was 6891.65 mIU per mL. Two hundred and fifty patients were managed surgically and 15 patients were treated by methotrexate. Table 2 summarizes the details of post-ectopic obstetric history. The average follow up was 30.74 ± 62.8 months.

Discussion. Our study shows an overall prevalence of EP of 1.13%, in our hospital that is higher than the reported from Saudi Arabia, but still within the general incidence from other parts of the world. The rate of ectopic pregnancies in North America increase from <0.5% of all pregnancies in 1970 to 2% in 1992¹⁸ but recent report suggests an incidence of 0.64%.¹⁹ Eskandar et al²⁰ after a review of 7 year admissions of EP from southern Saudi Arabia reported an incidence of 0.61%. Compared to these results our incidence is higher, this could be due to the increasing trend in EP. Several risk factors for EP have been identified and reported in the literature²¹⁻²³ and none of these factors have been studied in Saudi population. Advanced maternal age is long being blamed as a strong risk for EP,²⁴ but there is no general consensus on this. In our study, we found that parous women who had EP were significantly older (42.59 ± 7.9 versus 28.89 ± 5.7 years) than those who had other risk factors. It is possible that not only maternal age but age and previous pregnancies combined could play as an important risk factor. Another risk factor for EP is pregnancy achieved through assisted reproductive technology (ART). Bouyer et al²⁵ reported that infertility per se is associated with ectopic pregnancies and are considered high risk. Xiao et al²⁶ reported that in 2322 clinical pregnancies after ART, 4.1% of them ended in EP. In our own study, 47/259 EPs (18.2%) were on in vitro fertilization (IVF) or ovulation induction

(OI) protocols. It was highlighted that many post EP women develop secondary infertility.²⁷ Allonier et al²⁸ reported that many factors play a role in infertility after EP and the most important being the mode of surgical management. Al-Nuaim et al²⁹ reported 43.3% with a follow up of 12-60 months did not conceive. There is no recent data on this issue but our analysis shows that 27.7% of women in the reproductive age not being able to get pregnant. Tobacco smoking has been proved to be associated with EP. Several studies has shown to this effect.^{30,31} Bouyer et al²⁵ indicated that there is a dose-effect relation. In the conservative Saudi Arabian society women generally do not smoke, and if tobacco smoking has a detrimental effect, then, the incidence of EP should be much lower. Induced abortion was linked to EP under cloud of bias. Reports suggest a strong association of induced abortions and EP.³² The bias came with the link of 2 or more abortions which is claimed to increase the incidence of EP, and number of induced abortions may not be reported correctly by patients. The suggestion was induced abortion may lead to increase risk of abortions which in turn could trigger a higher risk of EP. In Saudi Arabia where induced abortions are neither permitted nor practiced routinely; we did not find any differences in incidence rates of EP in our study. Ectopic pregnancy recurrence after the first episode is not uncommon. De Bennetot et al³³ reported an incidence of 10.5%, while Aziz et al⁴ reported an incidence of 9% in a small study involving 66 patients. In this review, the incidence was 11.6% with an average follow up of 30.74 ± 62.8 (range 12-120 months).

Study limitation. The limitations, particularly of being a retrospective study. Secondly, we did not study the pelvic inflammatory disease as a cause of EP as it was not within the objectives of this study. Women in the early part of the study were not using IUCDs; thus, contraceptive methods details were not available in the medical charts. The strength of the study is the analysis of the patients included who were seen over a decade with long follow up and secondly the incidence of EP was calculated from more than 20,000 live births.

In conclusion, the prevalence of EP is higher than the reported small scale studies from Saudi Arabia. Age and increased number of previous pregnancies play an important risk factor for EP and Saudi women with IVF and OI patients are most likely to be prone. Lastly, the role of induced abortion and EP could be just coincidental.

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