

Studying the risk factors for ectopic pregnancy among spontaneous and assisted conception

Fakhir S. Al-Ani and Huda M. Mohammed

Department of Clinical Reproductive Physiology , High Institute of Infertility Diagnosis and Assisted Reproductive Technology/Al-Nahrain University.

Abstract:

background:

An ectopic pregnancy, or eccyesis, is a complication of pregnancy in which the pregnancy implants outside the uterine cavity. Theoretically, differences between conception via ART and natural conception may affect the risk of ectopic pregnancy. Data on the risk factors for developing ectopic pregnancy after IVF are still inconsistent. There is controversy whether ART increase or decrease the ectopic pregnancy.

Objectives:

To describe the occurrence or risk factors of ectopic pregnancy following IUI, IVF and spontaneous pregnancy

Patients and Methods:

The recorded cases of ectopic pregnancy in the period between January 2010 to January 2011 in four teaching hospitals and two private hospitals were surveyed. New cases in the period between July 2011 to July 2012 in two teaching hospitals were also included in this study. The data was collected from medical records and interview.

Results:

A total of 86676 pregnancies were recorded during the period of the study with, the number of ectopic pregnancy out of total pregnancies in Baghdad was 408 during the period of this study. It was found that the type of conception was significantly associated with infertility ($P < 0.001$), ovulation induction ($P < 0.001$), dilatation and curettage ($P = 0.016$), and history of contraception ($P = 0.002$).

Conclusion:

Although several risk factors for ectopic pregnancy are known, the causes of increasing incidence of ectopic pregnancy remain unknown. The risk factors of ectopic pregnancy following IUI, IVF and spontaneous pregnancy included history of infertility, medication used for ovulation induction, history of contraception, and dilatation curettage as these factors are tightly linked with the types of conception. Increasing knowledge of risk factors for ectopic pregnancy may improve understanding of the causes of infertility.

Key Words: Ectopic pregnancy, IUI, IVF, Risk factors

Introduction

An ectopic pregnancy, or *eccyesis*, is a complication of pregnancy in which the pregnancy implants outside the uterine cavity (1). The incidence of ectopic pregnancy has increased all over the world from 0.5% Thirty years ago, to a present day 12%-. Most ectopic pregnancies occur in the Fallopian tube (so-called tubal pregnancies), but implantation can also occur in the cervix, ovaries, and abdomen. An ectopic pregnancy is a potential medical emergency, and, if not treated properly, can lead to death. There are a number of risk factors for ectopic pregnancies. However, as many as one third (2) to one half of ectopic pregnancies, no risk factors can be identified. Risk factors include: pelvic inflammatory disease, infertility, use of an intrauterine device (IUD), previous exposure to DES, tubal surgery, intrauterine surgery (e.g. D&C), smoking, previous ectopic pregnancy, and tubal ligation(2).

Assisted reproductive technology (ART) is a general term referring to methods used to achieve pregnancy by artificial or partially artificial means. Examples of ART include *in vitro* fertilization, intracytoplasmic sperm injection (ICSI), cryopreservation, and intrauterine insemination (IUI) (3).

Data on the risk factors for developing ectopic pregnancy after IVF are still inconsistent. Between fresh non donor IVF and embryo transfer cycles, the significant risk factor for ectopic pregnancy was tubal factor infertility, and endometriosis, rather than male factor infertility. Higher ectopic pregnancy rate could be associated with zygote intrafallopian transfer, assisted hatching, large embryo transfer volume, deep fundal transfer, and frozen embryo transfer. . Higher implantation potential per embryo at the blastocyst stage may increase the risk of ectopic pregnancy than cleavage stage. Especially, according to numbers of embryos transferred, different risk of ectopic pregnancy after IVF was noted (4).

The aim of this study is to evaluate risk factors of ectopic pregnancy following IUI, IVF and spontaneous pregnancy.

Patients and Methods

The recorded cases of ectopic pregnancy in the period

between January 2010 to January 2011 in four teaching hospitals and two private hospitals were surveyed. Two teaching hospitals in Al-Karkh side: Al-Yarmouk and Al-Kadhymia Teaching Hospitals are included in this study as well as two teaching hospitals in Al-Rusafa side Al- Ulwya and Baghdad Teaching Hospitals and the two private hospitals: AL-Salama Hospital in AL-Karkh side and AL-Jarah hospital in Al-Rusafa side.

New cases in the period between July 2011 to July 2012 in two hospitals: Al-Kadhymia and Al-Yarmouk teaching hospitals were also included. In addition to the cases of IUI from the High Institute of Infertility Diagnosis and Assisted Reproductive Technology and IVF cases from private center for IVF in Baghdad.

This study is conducted to compare the risk factors of ectopic pregnancy among women who conceived after IVF and IUI and among women with spontaneous pregnancy. The data were collected from medical records and interview regarding patients age, parity, gestational age, ectopic pregnancy risk factors like history of previous abortion ,infertility treatment ,current use of intrauterine contraceptive device (IUD), history of previous tubal surgery (i.e. tubal ligation, sterilization reversal) history of appendectomy, caesarean section, appendicitis complicated by peritonitis, endometriosis, ovulation induction, IUI or IVF procedures (done in or outside the Iraq) , in addition to smoking habits, sexual and infectious history, characteristics of ectopic pregnancy , and the treatment procedure used.

Statistical analysis: The data were analyzed by using SPSS version 16 and Microsoft office 2007; numerical data were presented using Mean $\pm$ SD. Statistical tests used include: (Student t test used to compare the mean, chi square test used to compare the frequency, and Fish Exact test).P value <0.05 was considered significant.

Results

A total of 86,676 pregnancies were recorded during the period of the study with 408 pregnancies were outside the uterus proper as shown in table (1).

Table 1: Number and percentage of ectopic pregnancy from the total number of pregnancies included in the study.

	Ectopic	In topic	Total pregnancy
Number	408	86268	86676
Percent	0.47	99.53	100

The proportion of different types of conception: IVF, IUI and spontaneous conception among ectopic pregnancy is shown in table (2).

Table 2: Proportion of different types of conception among ectopic pregnancy.

Types of conception	Ectopic No. (%)	P Value
IVF	23 (5.64%)	<0.001
IUI	9 (2.20%)	
IVF & IUI	32 (7.84%)	
Spontaneous	376 (92.16%)	
Total	408 (100%)	

A significant association was found between different types of conception (IVF, IUI, and spontaneous conception) among ectopic pregnancy.

For the cases included, the mean age of the studied group and the mean age at marriage are shown in the table (3). There is a significant association between increasing age and types of conception ($P = 0.004$), while there is a non significant association between age at marriage and the types of conception ($P = 0.129$).

Table3: Mean age of studied group and mean age at marriage.

	Group1 (spontaneous)	Group2(IVF,IUI)	P value
Number	376	32	---
Mean age	30.04±6.42	32.72±4.66	0.004*
Mean age at marriage	25.38±5.20	23.89±4.95	0.129

*significant association between increasing age and types of conception.
The statistical test is (t- test).

Table4: Frequency of curettage in the studied group of pregnant women.

D&C	Group1 (spontaneous) No. (%)	Group2 (IVF or IUI) No. (%)	Total	P Value
No	282 (75%)	30 (94%)	312	0.016
Yes	94 (25%)	2 (6%)	96	
Total	376 (100%)	32 (100%)	408	

Statistical test is Chi-square test, $DF = 1$
Significant association was found between D&C and the types of conception.

There was a significant association between history of infertility and types of conception ($P < 0.001$) as shown in table (5).

Table4.5: Type of infertility in the studied group of ectopic pregnancy.

Infertility	Group1 (spontaneous) No. (%)	Group 2 (IVF,IUI) No. (%)	Total	P Value
No	258 (68%)	0 (0%)	258	<0.001
Yes	118 (32%)	32 (100%)	150	
Total	376 (100 %)	32 (100%)	408	

Statistical test is Chi-square test, DF =1

The mean duration of infertility for the studied cases is shown in table 6

(Table 6): Duration of infertility in the studied group.

	Group1(spontaneous)	Group 2(IVF,IUI)	P value
Number	118	32	---
Mean duration	3.68±2.55	5.89±3.54	0.004*

Significant association between duration of infertility & types of conception.*

Statistical test is(t- test).

The duration of infertility was significantly associated with types of conception as P=0.004

Table 7: Association between past history and types of conception.

Past history	Group1(spontaneous) No. (%)	Group2 (IVF or IUI) No. (%)	P value
Ovulation induction	147 (39%)	30 (94%)	<0.001*
PID	39 (10%)	2 (6%)	0.630 †
Surgery	58(15%)	7 (21%)	0.439 *
Previous EP	17 (5%)	4 (12.5%)	0.072 †
Contraception	73 (19%)	3(9%)	0.002*
Vaginal douching	49 (13%)	4 (13%)	1.000 †
Previous disease	5 (1%)	0(0%)	0.934 †
Smoking	22 (6%)	1(3%)	1.000 †

† Statistical test is Fisher Exact test

*Statistical test is Chi-square test

In this study a significant associations were found between types of conception and ovulation induction ($P < 0.001$) and contraception ($P = 0.002$). No significant association was found between types of conception and PID ($P = 0.630$), surgery ($P = 0.439$), previous EP ($P = 0.072$), vaginal douching ($P = 1.00$), previous disease ($P = 0.934$), and smoking ($P = 1.00$).

Discussion

In this study, there were significant increases in ectopic pregnancy following IVF and IUI as we found that the percentage of EP following IUI and IVF is (7.84%) from total EP, this is in agreement with other studies which were conducted by Farquhar (2). Similar finding were found by Laurie Barclay (3) who estimated a rate of EP after IVF between 2 and 11%. Clayton also found that the rate of EPs per 100 IVF births was 5% (4).

Nowadays, the increase in rate of EP following IVF and IUI is quiet happened. Increasing number of couples attending IVF center in addition to increasing acceptance of IVF/PGD as a method of sex selection are some of the attributable factors.

Different ART have different risk on the incidence of EP, as the rate of ectopic pregnancy in women undergoing IVF with transcervical transfer of fresh embryos is 2.2 %, and the rate is significantly increased (up to 3.6%) with zygote intrafallopian transfer (4), while with assisted hatching it reach 5.5 % as it was found by Jun et al. (5). These high rates were significantly decrease with donor oocytes as the risk is lower (1.6%) and when the embryos are transferred to a surrogate mother, the risk is 0.9% (6). One of the important determents factors for the outcomes in IVF is the time of embryo transfer. Lensy (7) found that difficult ET on day 2 rather than day 3 might increases the rate of EP, while Milki found that embryos transferred on day 3 and those on day 5 had similar rates of ectopic pregnancy (8). In addition to technique, the volume of embryo transfer media, the number and quality of embryos transfer could be determent factors that affect the rate of ectopic pregnancy as found by Weigert et al. (9). The medication used for ovulation induction might increase the risk as found by Shaista (10) and Cohen (11). Both researchers found that clomiphene citrate had two fold increase in the incidence of EP. With the use of gonadotropins the rate of ectopic pregnancies was 2.7% (12) and (13).

A question may rise here: Can this be prevented? The answer is no, since the exact mechanism and risk factors are not identified yet. The mechanism of implantation is just to be elucidated. What can be done is the early detection by serial β -hCG and early vaginal ultrasound scan then ectopic pregnancy can be treated medically before need for surgical intervention (14).

In the present study, many risk factors for EP were evaluated. Woman age was a significant risk factor for EP ($P = 0.004$), similar result was found by Bouyer (15). The association of ectopic pregnancy with increasing women age is likely due in part to an increased prevalence of fallopian tube scarring (16).

In this study significant association were found between types of conception and curettage ($P = 0.016$) because of increased prevalence of surgical evacuation of the retained product of conception due to the patient preference. There is also significant association between types of conception and duration of infertility ($P = 0.001$) and ovulation induction ($P = 0.001$). It was found that there is misuse of induction especially with clomid which may be used without medical consultation and in some cases and under social pressure, clomid is taken even when male factor is the cause of infertility (17). Other significant association was found between types of conception and contraception ($P = 0.002$). The injectable progesterone which affect the tubal motility, is more preferable by a considerable number of women due to their poor compliance with combined oral contraceptive pills. The same finding was found by Bouyer (15) who found also an association between EP and PID, previous ectopic, and surgery.

In this study, there were difficulties in determining the effect of female genital Chlamydial infection on reproductive outcome which arise from lack of uniform Chlamydia screening, a lack of sexual transmitted disease clinic and tracking, moreover lack of agreement on the diagnostic methods for diagnosis of Chlamydia infection (18).

Waylen (19) had found that cigarette smoking significantly increases the risk of tubal ectopic pregnancy as the nicotine in cigarettes stimulates contraction in the fallopian tubes and this can cause spasm resulting in temporary blockage of the tubes so the embryo cannot pass through, in addition to its damaging effect on the cilia of the fallopian tubes. The current study did not found association with smoking ($P = 1.0$). This may be explained by the fact that smoking in females in our community is not that prevalent as in the western communities, in addition some pregnant denied smoking due to social considerations.

In conclusion the increase impact of ectopic pregnancy in term of women risk and financial issues call for increase research about the causes of high prevalence of EP in order to act upon to reduce the risk and squally of ectopic pregnancy.

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