

Is there a relationship between age and side dominance of tubal ectopic pregnancies? – A preliminary report

Czy istnieje zależność pomiędzy wiekiem i stroną, po której umiejscawia się ciąża ektopowa jajowodowa? – doniesienie wstępne

Firat Okmen, Burak Zeybek, Ali Akdemir, Ahmet Mete Ergenoglu, Ozgur Yenieli, Murat Ulukus,

Ege University School of Medicine, Department of Obstetrics and Gynecology, Izmir, Turkey

Abstract

Objectives: To determine whether there exists a relationship between age and side dominance of tubal ectopic pregnancies.

Material and Methods: One hundred twenty patients were retrospectively analyzed. The sides of the tubal ectopic pregnancies were recorded on the basis of laparoscopy or laparotomy findings. Five age groups were created: 20-24, 25-29, 30-34, 35-39, and ≥ 40 years.

Results: Of the patients who were ≥ 30 years of age, 46 (69%) and 21 (31%) had tubal ectopic pregnancies on the right and left sides, respectively ($p=0.002$). In the 35-39 years of age group, 17 of 20 patients (85%) had tubal ectopic pregnancies on the right, and 3 of 20 patients (15%) on the left side ($p=0.002$). In the 30-34 years of age group, 26 of 39 patients (67%) and 13 of 39 patients (33%) had tubal ectopic pregnancies on the right and left sides, respectively ($p=0.037$). In the ≥ 40 years of age group, 3 of 8 patients (37%) had tubal ectopic pregnancy on the right side, while 5 patients (63%) on the left side ($p=0.48$).

Conclusions: Patients who are between the age of 30-40 years have a right-sided dominance of tubal ectopic pregnancy, however studies that involve larger numbers of subjects are needed to make definitive conclusions about women older than 40 years of age.

Key words: **ectopic pregnancy / side dominance / age / ovulation /**

Corresponding author:

Burak Zeybek
Ege University School of Medicine, Department of Obstetrics and Gynecology
Izmir, 35100, Turkey
Tel: +90 232 390 1700; Fax: +90 232 343 0711
e-mail: bzeybek@yahoo.com

Otrzymano: 15.11.2013
Zaakceptowano do druku: 14.03.2014

Firat Okmen et al. *Is there a relationship between age and side dominance of tubal ectopic pregnancies?*

Streszczenie

Cel pracy: Celem pracy była ocena czy istnieje związek pomiędzy wiekiem pacjentek i stroną, po której umiejscawia się ciąża ektopowa jajowodowa.

Materiał i metoda: Retrospektywnie przeanalizowano historię choroby 120 pacjentek. Umiejscowienie ciąży ektopowej było określone na podstawie laparoskopii lub laparotomii. Utworzono pięć grup wiekowych pacjentek: 20-24, 25-29, 30-34, 35-39 oraz >40 lat.

Wyniki: Spośród pacjentek w wieku ≥ 30 lat, 46 (69%) i 21 (31%) miało ciążę ektopową po prawej lub lewej stronie, odpowiednio ($p=0,002$). W grupie 35-39 lat, 17 z 20 pacjentek miało ciążę ektopową po prawej stronie a 3 (15%) po stronie lewej ($p=0,002$). W grupie 30-34 lat, 26 z 39 (67%) pacjentek oraz 13 z 39 (33%) miało ciążę po prawej lub lewej stronie, odpowiednio ($p=0,037$). W grupie kobiet powyżej 40 lat, 3 z 8 pacjentek (37%) miało ciążę ektopową po prawej stronie, podczas gdy 5 (63%) po stronie lewej ($p=0,48$).

Wnioski: Pacjentki w wieku 30-40 lat miały dominację prawostronnej ciąży ektopowej, aczkolwiek dalsze badania na większej grupie kobiet są potrzebne by wyciągnąć wnioski odnośnie kobiet powyżej 40 lat.

Słowa kluczowe: **ciąża ektopowa / dominacja strony / wiek / owulacja /**

Introduction

Ectopic pregnancy is defined as the implantation of the fertilized ovum outside the uterine cavity. Over 95% of all ectopic pregnancies are implanted in the fallopian tube [1]. That major health problem affects 1% of all pregnancies and is the most common cause of maternal mortality in the first trimester of pregnancy [2]. Although the main risk factors for tubal ectopic pregnancies, namely age, smoking, history of abortions, sexually transmitted diseases, infertility, and/or tubal surgeries, have been proposed, the exact mechanisms at the cellular and molecular levels are not fully understood due to the complexity of interactions between the fallopian tube and the embryo [3,4]. Patients with these risk factors may have structural and/or functional abnormalities of the fallopian tube which can impair the early embryo transport process and lead to tubal ectopic pregnancy [5].

To date many studies have been conducted to investigate the epidemiology, etiology, pathogenesis, diagnosis, and management of tubal ectopic pregnancies. However, to the best of our knowledge, the side dominance of tubal ectopic pregnancies and the relationship with age have not been studied. Thus, we attempted to determine whether there was a side dominance of tubal ectopic pregnancies and if it was age-related.

Objectives

To determine whether there was a relationship between age and side dominance of tubal ectopic pregnancies.

Methods

Our retrospective study involved 187 consecutive patients diagnosed at the Department of Obstetrics and Gynecology, Ege University School of Medicine with tubal ectopic pregnancy between January 2004 and October 2010. The diagnosis was made after measuring serial beta hCG levels with the concomitant use of transvaginal ultrasound. The data collected from the

patient charts included age, parity, fertility status, history of infertility treatments, tubal or abdominopelvic surgeries, pelvic infections, ectopic pregnancies, and the side of the tubal ectopic pregnancy. Patients with history of tubal surgeries ($n=9$), ectopic pregnancies ($n=11$), documented pelvic infections ($n=12$), and diagnosis/treatment of infertility ($n=8$) were excluded from the study. Twenty-seven patients diagnosed with ectopic pregnancy who were managed medically or expectantly were also excluded from the study. One hundred twenty patients were retrospectively analyzed (Figure 1). The side of the tubal ectopic pregnancies was recorded based on laparoscopy or laparotomy findings. Five patient groups were created according to age (20-24, 25-29, 30-34, 35-39, and ≥ 40 years).

Statistical evaluation was performed using descriptive statistical methods (mean, standard deviation [SD], and frequency) and chi-square tests. Differences were considered significant at the level $p<0.05$. The results are presented as mean \pm SD.

Results

Mean age of the patients was 30.48 years (range, 20-47 years). Age groups, number of patients within the groups, and side dominance of tubal ectopic pregnancies are shown in Table I.

Of patients who were ≥ 30 years of age, 46 (69%) and 21 (31%) had tubal ectopic pregnancies on the right and left sides, respectively ($p=0.002$). Of patients < 30 years of age, 23 (43%) and 30 (57%) had tubal ectopic pregnancies on the right and left sides, respectively ($p=0.33$; Table II).

When all age groups were considered, the most significant differences were noted in the 30-34 and 35-39 years of age groups. In the 35-39 years of age group, 17 of 20 patients (85%) had tubal ectopic pregnancies on the right side, and 3 of 20 patients (15%) on the left side. In the 30-34 years of age group, 26 of 39 patients (67%) had tubal ectopic pregnancies on the right side, and 13 of 39 patients (33%) on the left side.

Firat Okmen et al. *Is there a relationship between age and side dominance of tubal ectopic pregnancies?***Table I.** Number of patients in the age groups

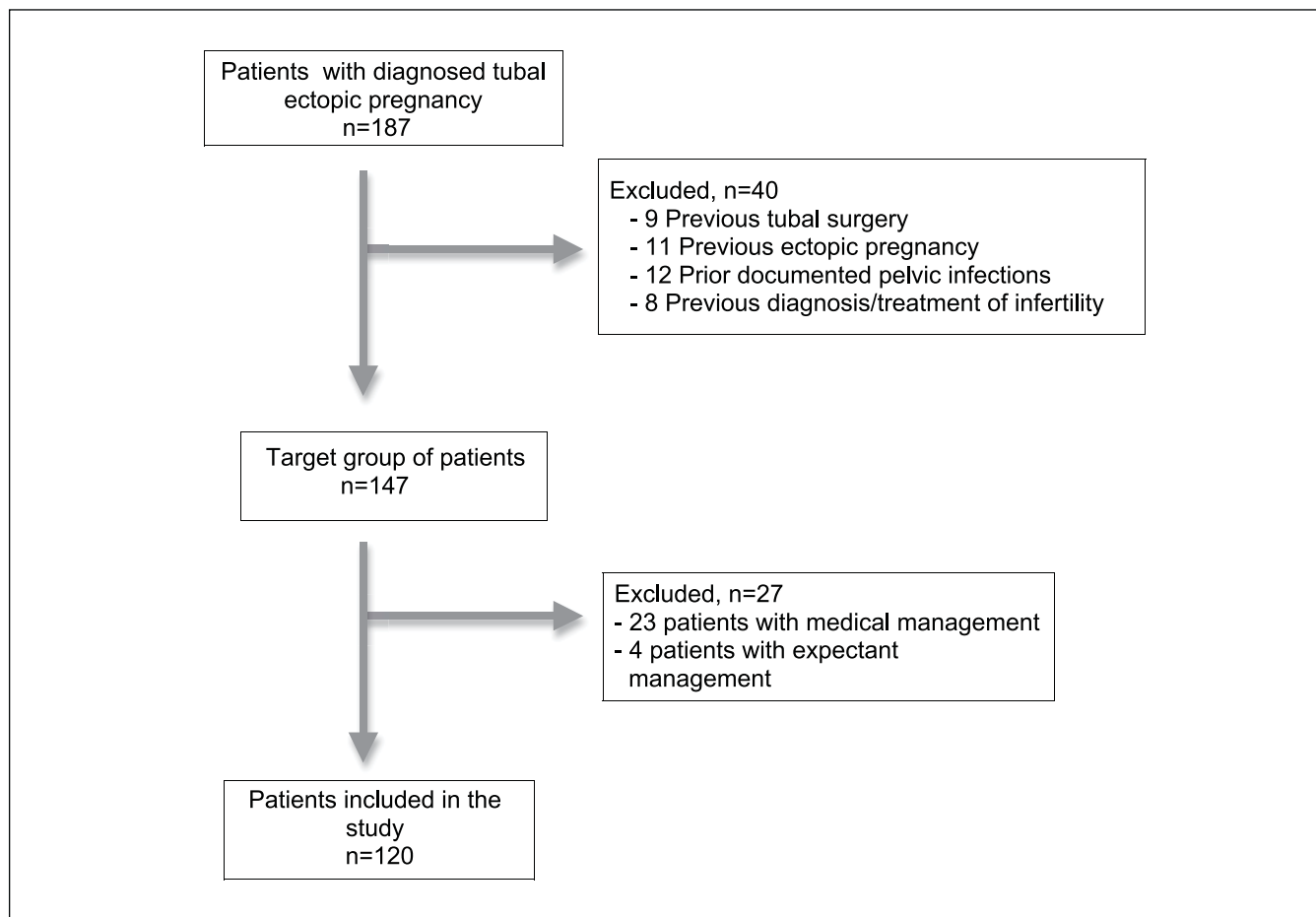
Age groups (years)	Right side tubal ectopic (n)	Left side tubal ectopic (n)	Total (n)	p value
20-24	7	12	19 (16%)	0.251
25-29	16	18	34 (28%)	0.732
30-34	26	13	39 (32%)	0.037†
35-39	17	3	20 (17%)	0.002†
≥ 40	3	5	8 (7%)	0.480
Total	69	51	120 (100%)	

† Statistically significant

Table II. The side of tubal ectopic pregnancies ≥ and < 30 years of age.

Age	Right side (n)	Left side (n)	p value
<30	23 (43.4%)	30 (56.6%)	0.336
≥30	46 (68.6%)	21 (31.4%)	0.002†
Total	69 (57.5%)	51 (42.5%)	0.1

† Statistically significant

**Figure 1.** The process of inclusion into the study.

Discussion

In order for a tubal ectopic pregnancy to occur, the ovulation must take place from one of the two ovaries, the fimbria must catch the ovum and fertilization must take place in the fallopian tube, and embryo-tubal transport must be impaired. It is the ovulation that determines the side dominance.

Despite numerous studies that investigated the ovulation characteristics of humans, the side of successive ovulations that favors pregnancy and the side sequence are still a matter of debate. Balasch et al., [6] analyzed 41 consecutive patients undergoing 156 *in vitro* fertilization cycles without ovarian stimulation. Fifty-two percent of the ovulations were on the right side; however, there was no statistical significance. Ecochard and Gougeon [7] studied 199 cycles in 80 healthy fertile women and reported that right-sided ovulation occurred in 104 of the 199 cycles (52.3%). Potashnik et al., [8] studied 97 follicles in 16 women who ovulated normally. Of the 97 follicles, 62 (64%) were detected in the right ovary, and the difference was found to be statistically significant. In the largest study in the literature, Fukuda et al., [9] evaluated over 2000 cycles, including both fertile and infertile women, and reported that the right ovary supports ovulation more frequently (55%) than the left ovary. Although these studies analyzed ovulation characteristics, the relationship between side dominance of the ovulation and age was not taken into consideration. To the best of our knowledge, there have been only two studies in the literature that investigated ovulation characteristics with reference to age. Jarvela et al., [10] analyzed ovulation side and cycle fecundity in frozen and thawed embryo transfer cycles. The cycles were spontaneous, with no hormonal treatment. In the study, ovulation was right-sided in 273 of the 477 cycles (57.2%) and left-sided in 204 of the cycles (42.8%) (95% CI 38.3-47.2, $p=0.002$). In addition, in the age group of 30-37 years, covering 288 cycles, the incidence of right-sided ovulation was 162 (57%), which was significantly higher than left-sided ovulation ($p=0.034$). In the study by Fukuda et al., [11], the frequency of ovulations from the right ovary in women < 29 years old was found to be 58%, 54% in the age groups of 30-34 and 35-39 years and 56% in women > 40 years of age. The overall average frequency was 55% and the difference was statistically significant.

In our study we found out that over the age of 30, especially between 35 and 39, the right ovary is the dominant side of ovulation. This is in agreement with findings of Fukuda et al., [11], who concluded that ovulation switching from one ovary to the other in two consecutive cycles (contralateral ovulation) was inversely correlated with age. In addition, Fukuda et al., [11] also showed that the ratio of right-sided ovulation per right-plus left-sided ovulations was unrelated to age and remained almost constant at a level of 55%. Our study also supports these results because no significant difference was found between the right and the left sided tubal ectopic pregnancies if all age groups were considered together. However, the ratio of the right-sided dominance was higher than left-sided dominance in the group of women over 30 years of age, and that difference was statistically significant. A conflicting result of our study, which was not in accordance with Fukuda et al., was that the left-sided dominance was found in patients over the age of 40. That might have been related to a small number of subjects in that age group, and the investigation should be repeated in larger populations. If all

age groups were considered together, no significant difference between right-and left-sided tubal ectopic pregnancies would be noted.

Based on the results of the current study, we conclude that there is a tendency for the right-sided ovulation to occur with increasing age or for the follicles from the right ovary to have a greater fertility potential than the follicles from the left ovary. The latter possibility can be explained by vascular differences between the two ovaries. The connection of the left ovarian and the left renal veins, which is generally more perpendicular than the connection between the right ovarian vein and the vena cava, may cause a reduced fertility potential of the oocytes from the left ovary due to the increased temperature in the left ovarian environment or the reflux of waste substances from the left renal vein. There is only one study in the literature [9] which investigated whether the fertility potential of one ovary is superior to the other. In this study, the implantation rate of pre-embryos originating from follicles from the right ovary (20%) was higher than the left ovary (13%), and the pregnancy rate per cycle of the right-sided ovulation was higher than the left-sided ovulation.

The clinical importance of our study lies in the fact that our findings could help draw the attention of clinicians to one side of the adnexa, especially in the case of very limited ultrasonographic findings. The initial stage of the disease is the golden period for successful medical therapy, however it is also the period in which very few clinical and ultrasonographic findings might occur. If the clinicians were aware of the possible dominance of the particular side, it would also be helpful during patient follow-ups.

Conclusion

In conclusion, patients who are between 30-40 years of age have the right-sided dominance of tubal ectopic pregnancies. The finding may be due to a higher frequency of right-sided ovulations or anatomic vascular differences of the two ovaries but the underlying mechanism is still unknown. Studies involving larger numbers of subjects are needed to make definitive conclusions about women over the age of 40.

Authors' Contribution

1. Firat Okmen – concept.
2. Burak Zeybek – article draft, corresponding author.
3. Ali Akdemir – collection of data, literature search.
4. Ahmet Mete Ergenoglu – data analysis, interpretation of data.
5. Ozgur Yeniel – data analysis, interpretation of data.
6. Murat Ulukus – concept.

Authors' statement

This is to certify, that the publication will not violate the copyrights of a third party, as understood according to the Act in the matter of copyright and related rights of 14 February 1994, Official Journal 2006, No. 90, Clause 63, with respect to the text, data, tables and illustrations (graphs, figures, photographs),

there is no 'conflict of interests' which occurs when the author remains in a financial or personal relationship which unjustly affects his/her actions associated with the publication of the manuscript,

Firat Okmen et al. *Is there a relationship between age and side dominance of tubal ectopic pregnancies?*

any possible relationship(s) of the author(s) with the party/parties interested in the publication of the manuscript are revealed in the text of the article, the manuscript has not been published in or submitted to any other journal.

Source of financing:

NONE.

References

1. Corpa JM. Ectopic pregnancy in animals and humans. *Reproduction*. 2006, 131, 631-640.
2. Varma R, Gupta J. Tubal ectopic pregnancy. *Clin Evid* (Online). 2009, Pii, 1406.
3. Pisarska MD, Carson SA, Buster JE. Ectopic pregnancy. *Lancet*. 1998, 351, 1115-1120.
4. Tay JJ, Moore J, Walker JJ. Ectopic pregnancy. *Br Med J*. 2000, 320, 916-919.
5. Farquhar CM. Ectopic pregnancy. *Lancet*. 2005, 366, 583-591.
6. Balasch J, Penarubia J, Marquez M, [et al.]. Ovulation side and ovarian cancer. *Gynecol Endocrinol*. 1994, 8, 7-12.
7. Ecochard R, Gougeon A. Side of ovulation and cycle characteristics in normally fertile women. *Hum Reprod*. 2000, 15, 752-755.
8. Potashnik G, Insler V, Meizner I, Sternberg M. Frequency, sequence and side of ovulation in women menstruating normally. *Br Med J*. 1987, 294, 219.
9. Fukuda M, Fukuda K, Andersen C, Byskov AG. Right-sided ovulation favours pregnancy more than left-sided ovulation. *Hum Reprod*. 2000, 15, 1921-1926.
10. Jarvela I, Nuojua-Huttunen S, Martikainen H. Ovulation side and cycle fecundity: a retrospective analysis of frozen/thawed embryo transfer cycles. *Hum Reprod*. 2000, 15, 1247-1249.
11. Fukuda M, Fukuda K, Andersen C, Byskov AG. Characteristics of human ovulation in natural cycles correlated with age and achievement of pregnancy. *Hum Reprod*. 2001, 16, 2501-2507.

KOMUNIKAT

GINEKOLOGIA, POŁOŻNICTWO

AKTUALNOŚCI 2014

Warszawa, 6 grudnia 2014 roku

Hotel Courtyard by Marriott, ul. Żwirki i Wigury 1

Przewodniczący Komitetu Naukowego:
prof. dr hab. n. med. Mirosław Wielgoś**Tematyka konferencji:**

- Ciąża wielopłodowa — jak wypracować standardy?
- Ginekologia — co nowego możemy zaoferować naszym pacjentkom?

Patronat

Patronat Medialny

Organizator



tvmed

VIA MEDICA

Szczegółowe informacje oraz rejestracja na stronie internetowej:

www.ginekologia.viamedica.pl

Konferencja jest skierowana do osób uprawnionych do wystawiania recept lub osób prowadzących obrót produktami leczniczymi — podstawa prawna: Ustawa z dnia 6 września 2001 r. Prawo farmaceutyczne (Dz.U. z 2008 r. nr 45, poz. 271).