

Sites of ectopic pregnancy: a 10 year population-based study of 1800 cases

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BACKGROUND: Several risk factors for ectopic pregnancy (EP) have been identified, but the site of implantation of EP has been little studied. **METHODS:** A total of 1800 surgically treated EP was registered between January 1992 and December 2001 in the Auvergne EP register and the women concerned were followed up. In this large population-based sample, we studied the distribution of EP sites, immediate complications, determining factors, and subsequent fertility. **RESULTS:** EP sites were interstitial (2.4%), isthmic (12.0%), ampullary (70.0%), fimbrial (11.1%), ovarian (3.2%) or abdominal (1.3%). No cervical pregnancies were observed. Complications and treatment depended on the site of EP. In multivariate analysis, the only risk factor associated with EP site was current use of an intrauterine device (IUD), which was more frequent in distal EP. The 2 year cumulative rate of subsequent spontaneous intrauterine pregnancy (IUP) increased progressively from interstitial to ovarian EP. Fair concordance (weighted $\kappa = 0.31$) was observed between the sites of two successive EP if they were homolateral. **CONCLUSION:** In addition to providing an accurate description of the sites of implantation of EP, this study shows that current IUD use 'protects' against interstitial pregnancies, which are the most difficult to manage. It shows that subsequent fertility tends to be higher in women with distal EP.

Key words: ectopic pregnancy/fertility/localization/population-based/recurrence

Introduction

During the 1980s and 1990s, the incidence of ectopic pregnancy (EP) in developed countries increased by a factor of three to four (Weström *et al.*, 1981; Atrash *et al.*, 1986; Chow *et al.*, 1987; Mäkinen, 1987; Anonymous, 1995) to reach 100 to 175 per 1 000 000 women aged 15–44 years. A decline in EP incidence has recently been observed in certain countries (Mäkinen, 1996; Coste *et al.*, 2000), but it remains unclear whether this trend also applies elsewhere, and could be attributed to decreases in genital infection rates (Egger *et al.*, 1998) or changes in contraceptive behaviour (Coste *et al.*, 2000).

Several risk factors for EP have been identified (Chow *et al.*, 1987; Coste *et al.*, 1991; Fernandez *et al.*, 1991a; Job-Spira *et al.*, 1993): pelvic inflammatory disease (PID)—especially for infections involving *Chlamydia trachomatis*—smoking, previous pelvic surgery, previous EP, past and current use of an intrauterine device (IUD).

The site of implantation of EP has been little studied, at least in large population-based samples. Only a few articles, published >15 years ago, report descriptive results concerning the site of EP in large samples either from populations defined geographically, (Hallatt, 1982; Hallatt and Grove, 1985; Atrash *et al.*, 1986; Herbertsson *et al.*, 1987) or from hospital-based

populations (Martin *et al.*, 1988; Al-Meshari *et al.*, 1993). The other studies on this subject are case reports or deal with very small series, with a review of previous studies. Moreover, all these papers focus on a specific site, none considering implantation of EP as a whole. To our knowledge, only one article has suggested a possible link between EP site and subsequent fertility (Pouly *et al.*, 1991) or EP recurrence, although improvements in the diagnosis and management of EP have shifted clinicians' concerns away from the immediate health of the woman, towards preserving her subsequent fertility.

The site of EP implantation merits study as it affects the severity of the condition, and the immediate and delayed side-effects. In addition, the effect of the site of implantation on subsequent fertility should be investigated.

The aim of this study was to investigate the distribution of EP sites in a population-based sample, and its variation over time. We then aimed to study the immediate complications and factors determining the site of EP. Finally, we determined the rates of subsequent fertility and EP recurrence.

Population and methods

Study population

The methodology of the Auvergne EP register has been described elsewhere (Coste *et al.*, 1994). Briefly, a register was established in

January 1992 in three *départements* (districts) of the Auvergne region in the centre of France (Allier, Cantal and Puy-de-Dôme). All women between 15 and 44 years of age who live permanently in the target area and who had had either surgical or medical treatment for EP were registered and followed up until the age of 45 years, all reproductive outcomes being recorded. In each medical centre in the area (15 public or private maternity hospitals and 12 surgical units) a trained investigator, either a midwife or a physician, was responsible for case identification, follow-up and data collection. The basic information collected for each woman included socio-demographic characteristics, sexual, gynaecological, reproductive and surgical history, conditions at conception (use of contraception, ovulation induction, IVF), smoking habits, results of serological tests for *Chlamydia trachomatis*, characteristics of the EP (site, tubal rupture, haemoperitoneum), and the treatment given. The completeness of the register has been estimated to be ~90% (Coste *et al.*, 1994, 2000).

The women were interviewed about reproductive events, by telephone, every 6 months after EP for 2 years, and then once per year until the age of 45 years. We asked questions about the desire for a new pregnancy, cumulative period of trying to become pregnant, pregnancies achieved, treatments for infertility and use of contraception.

This study was conducted on the 1933 EPs registered between January 1992 and December 2001. Women with medical treatment only ($n = 133$) were excluded from the study because the site of implantation could not be determined with certainty. Among the remaining 1800 subjects, the site of EP was determined by the operating surgeon and was known for 1679 subjects (93%), providing precise information concerning the distribution of EP implantation for this population-based sample. Six sites were recorded: interstitial part of the tube, isthmus, ampulla, fimbrium, ovary and abdomen.

For studies of subsequent fertility, we excluded the EP cases recorded in 2001 because we did not have enough time to record all the data for the first follow-up call for these cases. We also excluded 159 women who had undergone sterilization for contraception or therapeutic bilateral salpingectomy (with no desire for IVF). In addition, 133 women were lost to follow-up (8.7%). Thus, the analysis concerned 1228 women.

Factors studied and statistical methods

As very little is known about the factors determining the site of EP, we investigated the association between EP site and most of the known risk factors for EP. The treatment of EP was defined as radical if the tube in which the pregnancy occurred was removed, i.e. salpingectomy. Treatment was otherwise considered to be conservative. All French clinicians use similar guidelines when deciding between radical and conservative treatment (Pouly *et al.*, 1991). Haemoperitoneum of >100 ml was classified as profuse (Fernandez *et al.*, 1991c). We tested possible associations between EP site and these factors by means of χ^2 -tests and, when appropriate, χ^2 -tests for trend (Armitage and Berry, 1987) to take into account the ordered nature of the sites. Multivariate analyses were performed by multinomial logistic regression (Hosmer and Lemeshow, 2000).

Two reproductive outcomes were used to evaluate fertility: the recurrence of EP and intrauterine pregnancy (IUP). In both cases, survival analysis methods were used with person-time being the time to pregnancy. This is the cumulative period of time during which a woman was trying to become pregnant until she became pregnant or was censored. Cumulative rates and confidence intervals (CI) were calculated by the Kaplan–Meier estimator (Breslow and Day, 1987) for each of the sites. The curves obtained were compared by log-rank tests for univariate analysis, and by Cox regression (Cox and Oakes, 1990) to take into account confounding variables. Ties in time to pregnancy data were handled using a published method (Efron,

1977). The confounding factors had been identified as being associated with subsequent fertility either in our previous analyses (Job-Spira *et al.*, 1996; Bernoux *et al.*, 2000) or by other teams (Thorburn *et al.*, 1988; Yao and Tulandi, 1997): age, educational level, prior tubal damage, history of infertility, tubal rupture and treatment (conservative or radical). For women with several successive pregnancies, the time to pregnancy was calculated until the first occurrence of the type of pregnancy studied (EP or IUP). Only 'natural' fertility was studied, and follow-up was censored if a woman began an IVF programme or had declared that she was not trying to become pregnant again (Bernoux *et al.*, 2000). In terms of methodology, there is no entirely satisfactory way to take IVF into account because this event is not independent of a woman's fertility (IVF is prescribed for less fertile women). The removal of women undergoing IVF from the sample analysed would therefore result in an overestimate of fertility. Moreover, such exclusion is always incomplete because we cannot identify women who will undergo IVF treatment in the future. In our study, we censored follow-up only when the woman actually underwent IVF. Thus, we did not exclude the entire follow-up period for women undergoing IVF, limiting the overestimation of infertility.

In cases of EP recurrence, we investigated whether the sites of the two successive EP were identical or close to one another, by calculating weighted κ -statistics (Fleiss, 1981). κ -statistics are parameters of agreement that take chance agreement into account (agreement or concordance between the sites of the two EP in this study). The weighted κ -statistic is based on the idea that if two sites differ by more than one category, then the disagreement should be given more weight than if they differ by only one category. Quadratic (dis)agreement weights were used. Values of $\kappa > 0.8$ indicate almost perfect agreement, values of 0.6–0.8 indicate substantial agreement, with 0.4–0.6 indicating moderate agreement, 0.2–0.4 fair agreement, and < 0.2 poor agreement (Landis and Koch, 1977).

Statistical analyses were performed with STATA software (Stata-Corp, 2001).

Results

Distribution of EP sites

The distribution of the sites of ectopic pregnancy is given in Table I. Only 4.5% extratubal EPs (ovarian and abdominal) were observed and about three-quarters of the tubal pregnancies (1175/1603 = 73%) were ampullary. No cervical pregnancies were observed. The 95% confidence interval (CI) of the proportion of EPs accounted for by cervical pregnancies is thus 0–0.0022. Thus, cervical EPs are probably very rare, accounting for ≤ 1 in 455 EP. The distribution of implantation sites varied over time ($P = 0.04$). This variation was accounted for mostly by increases in the proportion of interstitial and isthmus EP. These increases were also accounted for by a decrease in the number of women using IUD at the time of EP (as shown below, IUD use is associated with EP site). Similar results were obtained if we excluded the period 2000–2001, in which the proportion of medical treatments was higher (and thus the proportion of undetermined sites of EP was higher).

Clinical features and management

The proportion of cases of EP diagnosed before 6 weeks gestation increased significantly from interstitial to abdominal EP sites (Table II). This trend remained significant after adjust-

Table I. Distribution of the sites of ectopic pregnancy (EP): Auvergne register (France) 1992–2001

	Interstitial	Isthmic	Ampullary	Fimbrial	Ovarian	Abdominal	Total
<i>n</i>	41	201	1175	186	54	22	1679
%	2.4	12.0	70.0	11.1	3.2	1.3	
Variations across 2 year time periods ^a							
1992–1993	1.2	11.1	72.1	10.3	2.4	2.9	341
1994–1995	1.8	9.0	73.6	12.1	2.6	0.8	387
1996–1997	3.0	11.1	70.3	10.1	5.1	0.7	297
1998–1999	4.2	14.0	65.3	12.5	3.6	0.6	337
2000–2001	2.2	15.1	68.1	10.1	2.8	1.6	317

^a $P < 0.04$ for the comparison between the distributions of EP sites.

Table II. Clinical features and management of ectopic pregnancy (EP) according to site: Auvergne EP register (France) 1992–2001

	Total	Interstitial	Isthmic	Ampullary	Fimbrial	Ovarian	Abdominal	<i>P</i>
<i>n</i>	1679	41	201	1175	186	54	22	
Diagnosis before 6 weeks	620 (40.7)	12 (32.4)	75 (40.5)	520 (39.7)	75 (43.1)	27 (54.0)	11 (55.0)	0.03 ^a
Tubal rupture	259 (16.0)	13 (36.1)	46 (23.7)	178 (15.7)	22 (12.2)	0	0	0.001
Profuse haemoperitoneum	494 (29.9)	12 (31.6)	67 (33.7)	318 (27.4)	66 (36.1)	23 (42.6)	8 (36.4)	0.03
hCG concentration (IU/l)								0.01 ^b
Mean	4023	10 605	5058	3722	3210	5317	1408	
SD	8 773	21 060	9734	8169	5684	9774	2077	
First treatment conservative	921 (54.9)	21 (51.2)	98 (48.8)	622 (52.9)	122 (65.6)	39 (72.2)	19 (86.4)	0.001
First treatment failure	119 (7.1)	6 (14.6)	16 (8.0)	70 (6.0)	21 (11.3)	5 (9.3)	1 (4.6)	0.04
Final treatment conservative	881 (52.5)	17 (41.5)	92 (45.8)	596 (50.7)	118 (63.4)	39 (72.2)	22 (86.4)	0.001

Values in parentheses are percentages of each factor according to the site.

^aTest for trend.

^bComparison of the means of ln(hCG) concentration.

ment for tubal rupture or haemoperitoneum, the frequency of which also depended on the site of EP. Adjustment for haemoperitoneum also made it possible to take into account, at least partly, possible errors in gestational age due to metrorrhagia early in the pregnancy. Concentrations of hCG, an indicator of pregnancy activity, decreased progressively from interstitial to abdominal EP sites, and this trend remained significant after adjustment for pregnancy term at the time of diagnosis.

The proportion of EP initially managed conservatively increased progressively from interstitial to abdominal EP sites. Moreover, the increase over time in the proportion of EP treated conservatively was larger for interstitial sites than for any other location. The first treatment was considered to have failed if the clinician decided to treat the woman again for the same EP, either medically or surgically. Differences in the rates of failure of the first treatment were accounted for mostly by a high proportion of failure in interstitial (14.6%) and fimbrial (11.3%) EP.

Results similar to those in Table II were obtained if the main characteristics of the women (such as age, smoking, previous sexually transmitted disease, current IUD use and educational level) were taken into account as potential confounders.

Determinant factors

The relationship between EP site and the characteristics of the woman is shown in Table III. The association with current use of an IUD was particularly strong: the proportion of IUD users

increased from interstitial to ovarian sites (in the population studied, about one woman in three was a current IUD user). However, the distribution of EP sites was similar in women who had used an IUD only in the past and women who had never used an IUD.

A history of damaged tubes (as shown by a history of EP or tubal surgery) was more frequent in women with proximal implantation than in those with distal implantation. This association was similar regardless of the side of the body on which previous EP had occurred (contralateral or homolateral). The other factors studied, including those not shown in Table III (educational level, previous induced abortion, history of infertility and induction of the pregnancy), were not associated with EP site.

In multivariate analysis, the only factor that remained significantly associated with EP site was current use of an IUD, although prior EP was also close to the significance threshold.

Subsequent fertility

For the 1228 women followed up, mean follow-up time was 3.2 years, and 693 women had tried to become pregnant again. It was not possible to study subsequent fertility among women with an abdominal pregnancy because only nine of these women had tried to become pregnant again. Of the remaining 684 women, 78 experienced another EP. The 2 year cumulative rate of recurrent EP was 0.22 (95% CI 0.17–0.28). No

Table III. Distribution of the potential determinant factors of the site of ectopic pregnancy (EP): Auvergne EP register (France) 1992–2001

	Total	Interstitial	Isthmic	Ampullary	Fimbrial	Ovarian	Abdominal	P-values ^a	
								P1	P2
<i>n</i>	1679	41	201	1175	186	54	22		
Age (years)									
<25	210 (12.5)	4 (9.8)	16 (8.0)	157 (13.4)	24 (12.9)	6 (11.1)	3 (14.3)	NS	NS
25–29	454 (27.1)	8 (19.5)	58 (28.9)	314 (26.8)	53 (28.5)	16 (29.6)	5 (23.8)		
30–34	523 (31.2)	14 (34.2)	73 (36.3)	362 (30.8)	51 (27.4)	16 (29.6)	7 (33.3)		
≥35	490 (29.2)	15 (36.6)	54 (26.9)	341 (29.1)	58 (31.2)	16 (29.6)	6 (28.6)		
Smoker	767 (48.1)	22 (59.5)	97 (51.3)	530 (47.4)	83 (46.6)	26 (50.0)	9 (42.9)	NS	NS
Current IUD	424 (25.5)	3 (7.5)	43 (21.5)	281 (24.1)	67 (36.2)	23 (43.4)	7 (31.8)	0.001	0.001
Prior delivery	1164 (69.7)	28 (68.3)	150 (75.0)	796 (68.2)	132 (71.0)	43 (81.1)	15 (68.2)	NS	NS
Prior spontaneous abortion	428 (25.6)	10 (24.2)	55 (27.5)	307 (26.3)	37 (19.9)	15 (28.3)	4 (18.2)	NS	NS
Prior EP	210 (12.6)	11 (26.8)	31 (15.5)	146 (12.5)	13 (7.0)	6 (11.3)	3 (13.6)	0.02	0.09 (NS)
Prior STD ^b	318 (19.7)	9 (23.7)	32 (16.6)	241 (21.3)	24 (13.6)	8 (15.1)	4 (18.2)	NS	NS
Prior tubal surgery	312 (18.7)	13 (31.7)	43 (21.5)	220 (18.8)	21 (11.3)	10 (18.9)	5 (22.7)	0.03	

Values are absolute numbers (percentages in parentheses) for each factor according to site.

^aP1 = *P*-value in univariate analysis; P2 = *P*-value in multivariate analysis (including all variables except prior tubal surgery).

^bProbable pelvic inflammatory disease (PID), association of fever, abdominal pain and vaginal discharge; and/or PID confirmed by laparoscopy, and/or positive serological tests for *Chlamydia trachomatis*.

IUD = intrauterine device; STD = sexually transmitted disease; NS = not significant.

Table IV. Subsequent fertility according to the site of the index ectopic pregnancy (EP) (among women trying to become pregnant again): Auvergne EP register (France) 1992–2001

	Total	Interstitial	Isthmic	Ampullary	Fimbrial	Ovarian	<i>P</i>
No. of women trying to become pregnant again	684	16	88	489	73	18	
Recurrent EP							
No.	78	1	10	60	6	1	
2 year cumulative rate	0.22	0.08	0.24	0.23	0.14	0.13	NS ^a
95% CI	0.17–0.28	0.01–0.43	0.11–0.48	0.17–0.30	0.05–0.33	0.02–0.61	
Intrauterine pregnancy							
No.	411	8	52	286	50	15	
2 year cumulative rate	0.76	0.71	0.71	0.75	0.84	0.83	0.08 ^b (NS)
95% CI	0.71–0.80	0.44–0.93	0.58–0.83	0.69–0.80	0.72–0.93	0.63–0.96	

^aLog-rank test between the five sites.

^bTest for trend.

CI = confidence interval; NS = not significant.

significant differences in EP recurrence rates were observed according to the site of the current EP (Table IV).

The 2 year cumulative rate of IUP was 0.76 overall [95% CI (0.71–0.80)], and increased progressively from interstitial to ovarian EP sites (Table IV and Figure 1), with a test for trend giving a *P*-value close to the threshold of statistical significance (*P* = 0.08). However, this crude trend was partly accounted for by confounding (adjusted test for trend *P* = 0.38), in particular by the larger proportion, among cases of ovarian and fimbrial EP, of women with an IUD, whose subsequent fertility is known to be better (Bernoux *et al.*, 2000).

If we considered all the women (whether or not they had tried to become pregnant), 113 had had another EP. The sites of the two successive pregnancies were known for 99 women and two of these pairs of EP included one abdominal EP. Fair concordance was observed between the sites of implantation if the two EPs were homolateral (weighted κ = 0.31; *P* < 0.01; Table V). Conversely, no concordance was observed if the two EPs were contralateral (weighted κ = –0.03; *P* = 0.58).

The women with homolateral recurrent EP were slightly older than those with contralateral recurrent EP. However, we found no significant differences for any of the other characteristics of the women, including infectious history.

Discussion

Almost all the women living in the Auvergne region who were treated for EP between January 1992 and June 2001 were included in this study, the completeness of the Auvergne EP register being estimated to be ~90% (Coste *et al.*, 1995, 2000). The characteristics of the index EP were collected prospectively. Women were also interviewed every 6 months after EP about their seeking to become pregnant again and fertility outcome, and few (8.7%) were lost to follow-up. Thus, selection and recall biases, which frequently occur in retrospective studies with hospital recruitment, were probably very limited. The proportion of medical treatments increased with time. Therefore, the number of EP for which the site was

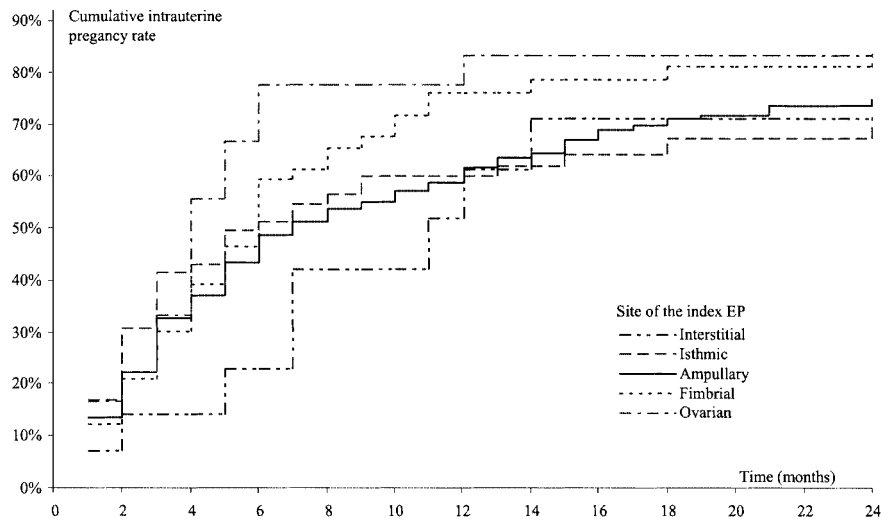


Figure 1. Cumulative intrauterine pregnancy rates according to the site of the ectopic pregnancy (EP) (among women trying to become pregnant again): Auvergne EP register (France) 1992–2001.

Table V. Sites of the two successive ectopic pregnancies (EP) among women with recurrent EP: Auvergne EP register (France) 1992–2001

Recurrent EP	First EP					
	Interstitial	Isthmic	Ampullary	Fimbrial	Ovarian	Total
Homolateral EP (weighted $\kappa = 0.31$; $P = 0.01$)						
Interstitial			1			1
Isthmic			6			6
Ampullary		2	23	2		27
Fimbrial			3	2		5
Ovarian				1		1
Total	0	2	33	5	0	40
Contralateral EP (weighted $\kappa = -0.03$; $P = \text{NS}$)						
Interstitial		1	2			3
Isthmic		1	5			6
Ampullary		8	31	3	1	43
Fimbrial		1	2			3
Ovarian		1	1			2
Total	0	12	41	3	1	57

NS = not significant.

not determined also increased, and was especially large in the last period studied (2000–2001). However, we obtained similar results if we excluded this period.

Some abdominal pregnancies are not primary abdominal pregnancies, but result instead from ruptured tubal or ovarian pregnancies (Hallatt and Grove, 1985; Costa *et al.*, 1991; Dover and Powell, 1995). Even if the primary site of implantation of such pregnancies was known (for instance fimbrium), we classified them as abdominal because they could not be considered to be similar to other fimbrial EP: even if only secondarily, their implantation was abdominal (Martin *et al.*, 1988). We therefore retained the ‘abdominal’ category and studied the characteristics of EP for all six sites.

Few articles describing the distribution of all EP implantation sites have been published. Moreover, the distribution is often cited with respect to all pregnancies, rather than with respect to EP, and may therefore vary according to the proportion of EP among pregnancies. Most of the remaining papers are

devoted to specific sites (mainly interstitial, ovarian or abdominal EP), often studied from hospital-based data. However, the published figures are consistent with those reported here: 3–11% for interstitial EP (Fernandez *et al.*, 1991b; Kabukoba and de Courcy-Wheeler, 1992; Khalifa *et al.*, 1994; Tulandi *et al.*, 1995); 1–6% for ovarian EP (Gérin-Lajoie, 1951; Boronow *et al.*, 1965; Hallatt, 1982; Grimes *et al.*, 1983; Steiner *et al.*, 1983; Herbertsson *et al.*, 1987; Sandvei *et al.*, 1987; Cabero *et al.*, 1989; Raziel *et al.*, 1990; Al-Meshari *et al.*, 1993; Chahtane *et al.*, 1993); 0.9–1.4% for abdominal EP (Radman, 1978; Delke *et al.*, 1982; Atrash *et al.*, 1987).

An increase in the incidence of ovarian EP over time has been reported (Steiner *et al.*, 1983; Sandvei *et al.*, 1987; Cabero *et al.*, 1989; Raziel *et al.*, 1990). Some authors account for this increase by improvements in diagnosis (Cabero *et al.*, 1989; Raziel *et al.*, 1990). This is consistent with our observations because the incidence of ovarian EP increased until 1997, with the proportion of ovarian EP remaining fairly steady

thereafter. Another possible interpretation is based on the role of IUD in interfering with the transport of ova from the ovary into the tube and variations in IUD use over time (Herbertsson *et al.*, 1987). This interpretation is not supported by our observations because IUD use has decreased in the Auvergne region since 1992 (Coste *et al.*, 2000).

We observed that the increase over time in the proportion of EP treated conservatively was greater for interstitial EP than for EP at other sites. This is consistent with the fact that before the 1990s, interstitial pregnancy was treated by cornual resection or hysterectomy probably due to late diagnosis in many cases (Parente *et al.*, 1983; Tulandi *et al.*, 1995). Since then, advances in transvaginal sonography and in medical treatment with methotrexate have opened up new avenues for conservative treatment by laparoscopy (Fernandez *et al.*, 1991b).

In multivariate analysis, the only factor significantly associated with the site of EP was current contraception with an IUD, which was more frequent in distal EP cases. This is consistent with previous findings (McMorries *et al.*, 1979; Hallatt, 1982; Sandvei *et al.*, 1987; Raziel *et al.*, 1990). The IUD may cause mild inflammation, resulting in deciliation of the endosalpinx and therefore delayed ovum transport, leading to ectopic implantation (Herbertsson *et al.*, 1987). This finding both confirms the role of IUD in the aetiology of EP (Bouyer *et al.*, 2000), and suggests that there may be tubal factors involved in the aetiology of ovarian pregnancy (Sandvei *et al.*, 1987). IUD seem to play a role only in the short term, because no association with the site of EP was found if the woman had used an IUD only in the past.

The higher proportion of women with markers of tubal damage, such as previous EP or previous tubal surgery, that we found in proximal EP cases is consistent with previous reports (Boronow *et al.*, 1965; Herbertsson *et al.*, 1987; Cabero *et al.*, 1989; Raziel *et al.*, 1990; Yarali *et al.*, 1994; Lau and Tulandi, 1999), but this association was found to be weaker after adjustment for other determinant factors. Moreover, similar results were obtained regardless of the site of the previous EP (homo- or contralateral), suggesting that tubal surgery *per se* did not determine the location of a subsequent EP.

The crude difference in subsequent fertility observed between sites was close to the threshold of statistical significance and became non-significant if conservative treatment was considered. It is therefore possible that subsequent fertility does not depend on the EP site. However, as treatment was more frequently conservative in cases of distal EP, we cannot rule out the possibility that treatment plays the role of an intermediate factor between EP site and subsequent fertility. This would imply that the site itself plays a role, as previously suggested for ovarian pregnancies (Boronow *et al.*, 1965; Hallatt, 1982; Raziel *et al.*, 1990).

The concordance between the sites of recurrent homolateral EP, but not between the sites of contralateral EP, is interesting. As the infectious histories of women with homo- and contralateral EP were similar, this result suggests that surgical treatment of the tube may induce recurrence at the same location. In cases of conservative management of EP, this, in

turn, may be an argument for favouring medical treatment whenever possible.

This study is the first to describe the sites of implantation of EP in a large population-based sample. It confirms that the complications of EP vary considerably according to site. It shows that current IUD use 'protects' against interstitial pregnancies, which are the most difficult type of EP to manage. Finally, it shows that subsequent fertility tends to be higher for distal and extratubal EP and that there is fair concordance between the sites of two successive EP if they are homolateral.

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