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Pregnancy rates after in-vitro fertilization in cases of tubal infertility with and without hydrosalpinx: a meta-analysis of published comparative studies

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This meta-analysis was intended to evaluate differences in pregnancy rates after in-vitro fertilization (IVF) in tubal fertility with and without hydrosalpinx. It examined nine published retrospective comparative series and five series published as abstracts for which additional information was obtained. In all, these studies involved 5592 patients (1004 with hydrosalpinx and 4588 with tubal infertility without hydrosalpinx). The main outcome measures were rates of pregnancy, implantation, live delivery, and early pregnancy loss. Pregnancy rates were significantly lower in the presence of hydrosalpinx: 31.2% for the tubal sterility group without hydrosalpinx and 19.7% for the group with hydrosalpinx (odds ratio: 0.64; 95% confidence interval: 0.56, 0.74). Similarly, the implantation rate and the delivery rate per transfer in the hydrosalpinx group were only slightly more than half those of the non-hydrosalpinx group (implantation: 8.5 and 13.7%, respectively; delivery: 13.4 and 23.4%). The incidence of early pregnancy loss was also higher in the hydrosalpinx group (43.7%) than in the control group (31.1%). This meta-analysis makes it clear that hydrosalpinx present during IVF–embryo transfer has negative consequences on the rates of pregnancy, implantation, live delivery, and early pregnancy loss. It would be premature, nonetheless, to conclude that routine salpingectomy should be performed on all patients with hydrosalpinx.

Key words: hydrosalpinx/implantation rate/IVF/pregnancy rate

Introduction

Tubal infertility is one of the major indications for in-vitro fertilization (IVF). For these cases, many factors affect the IVF results, including the patient's age, the quality of the ovarian stimulation, the quality and number of embryos transferred, and the ultrasound appearance of the endometrium. The cause of the tubal infertility is also an important factor influencing IVF results. Recent reports have examined potentially deleterious effects of uni- or bilateral hydrosalpinx. However, there is no current therapeutic consensus about the presence of hydrosalpinx at the time of inclusion in an IVF programme. We decided that a meta-analysis of published series was necessary to evaluate the consistency of published results and enable patients to receive better information about their prognosis for IVF in the presence of hydrosalpinx. With meta-analysis, more subjects are available for analysis so that small differences can be detected, and the rationale for certain therapeutic decisions can be clarified.

Materials and methods

Research and data selection

We performed a search of Medline and the Cochrane Database of Systematic Reviews. The references of the pertinent articles were then in turn reviewed. This analysis includes only studies in which the patients' infertility was attributed to tubal causes; it compares a group of patients with uni- or bilateral hydrosalpinx with a group without hydrosalpinx.

The data included in this meta-analysis came from nine published retrospective comparative series with sufficient data (Andersen *et al*., 1994; Strandell *et al*, 1994; Van Dromme *et al*., 1995; Akman *et al*., 1996; Fleming and Hull, 1996; Katz *et al*., 1996; Sharara *et al*., 1996; Blazar *et al*., 1997; Wainer *et al*., 1997) and five series published as abstracts for which we obtained additional information directly from the authors (Sims *et al*., 1993; Murray *et al*., 1996; Barmat *et al*., 1997; Ng and Ho, 1997; De Witt *et al*., 1997).

Six series were rejected. Three lacked data for the criteria under study, even after correspondence with the authors (Freeman *et al*., 1995; Claman *et al*., 1997; Fukui *et al*., 1997). One randomized, prospective study included patients with tubal disease who were randomized in terms of salpingectomy versus no salpingectomy, but patients with hydrosalpinx were not categorized separately (Dechaud *et al*., 1995). The series reported by Kassabji *et al.* (1994) was not included because the populations studied were a sub-population of that reported by Sims *et al*. (1993). In addition, one consecutive series compared the same patients before and after salpingectomy (Shelton *et al*., 1996).

The number of patients and cycles in the 14 retrospective series that were included are shown in Table I. The series were published between 1994 and 1997. The total number of patients included in this meta-analysis is 5592: 1004 were in the hydrosalpinx group, and 4588 in the group with tubal infertility without hydrosalpinx. The total number of transfers performed was 8703: 1642 in the hydrosalpinx group and 7061 in the group without hydrosalpinx. Data collection from the various studies was arbitrarily stopped in June 1997.

Definitions of the populations studied

The populations consisted of consecutive cases treated in infertility treatment centres. Some of our outcome measures could not be determined from the published results of some of the series. After corresponding with the authors, however, we were able to obtain the

Table I. Studies comparing groups with hydrosalpinx to groups with tubal infertility without hydrosalpinx

First author and year of publication	Groups with hydrosalpinx			Groups without hydrosalpinx		
	No. of women	No. of transfers	Diagnostic criteria	No. of women	No. of transfers	Inclusion criteria
Andersen (1994)	62	91	Echo	493	744	Tubal infertility, all causes
Strandell (1994)	45	121	HSG and/or laparoscopy	173	367	Tubal infertility, all causes
Sims (1993)	118	234	HSG and/or laparoscopy	823	1287	Tubal infertility, all causes
Blazar (1995)	67	155	Echo and/or HSG laparoscopy	183	359	Tubal infertility, all causes
Van Dromme (1995)	37	69	HSG and/or laparoscopy	41	61	Bilateral salpingectomy or tubal ligation
Sharara (1996)	63	103	HSG and/or laparoscopy	60	89	Tubal infertility, all causes
Akman (1996)	10	14	Echo and/or HSG laparoscopy	74	98	Tubal infertility, all causes
Murray (1996)	26	45	HSG and/or laparoscopy	90	141	Tubal infertility, all causes
Katz (1996)	79	95	Echo and/or HSG laparoscopy	812	1268	Tubal infertility, all causes
Fleming (1996)	79	77	HSG and/or laparoscopy	220	212	Tubal infertility, all causes
Wainer (1997)	91	267	Echo and/or HSG laparoscopy	352	867	Tubal infertility, all causes
Barmat (1997)	60	106	Echo and/or HSG laparoscopy	940	1150	Tubal infertility, all causes
Ng (1997)	43	41	HSG and/or HSG laparoscopy	101	92	Tubal infertility, all causes
De Witt (1997)	224	224	Echo and/or laparoscopy	326	326	Tubal infertility, all causes
Total	1004	1642		4588	7061	

HSG = hysterosalpingography.

necessary data. The populations of the various groups and the measures for analysis were defined as follows.

Only one series distinguished between unilateral and bilateral hydrosalpinx in its results (Wainer *et al*., 1997). For the sake of homogeneity, therefore, we consolidated the unilateral and bilateral groups from that study. The percentage of bilateral hydrosalpinx in the hydrosalpinx group was known in only two series: 22.5% in Andersen *et al*. (1996) and 59.3% in Wainer *et al*. (1997). The diagnosis of hydrosalpinx was made either by ultrasound alone (Andersen *et al*., 1994; Barmat *et al*., 1997), or by hysterosalpingography and/or laparoscopy (Strandell *et al*, 1994; Fleming *et al*., 1996; Murray *et al*., 1996; Sharara *et al*., 1996), or by any one of these three examinations (Akman *et al*., 1996; Katz *et al*., 1996; Blazar *et al*., 1997; De Witt *et al*., 1997; Ng *et al*., 1997; Wainer *et al*., 1997).

The control group consisted of patients with tubal infertility without hydrosalpinx. Some authors included all cases of tubal infertility at their centre (Sims *et al*., 1993; Andersen *et al*., 1994; Strandell *et al*., 1994; Katz *et al*., 1996; Sharara *et al*., 1996; Barmat *et al*., 1997; Blazar *et al*., 1997; De Witt *et al*., 1997; Ng and Ho, 1997; Wainer *et al*., 1997). Van Dromme *et al*. (1995) included only those cases of tubal infertility in which there was a history of bilateral salpingectomy or tubal ligation. Andersen *et al*. (1994) compared four groups of patients, but two of the groups are not included in our analysis. One group had tubal infertility with an unclear diagnosis of hydrosalpinx, and the other had non-tubal infertility. In the series reported by Murray *et al*. (1996), we did not analyse groups III and IV because they included patients treated surgically for hydrosalpinx. Strandell *et al*. (1994) studied two control groups of patients with tubal infertility without hydrosalpinx; however, the diagnosis of hydrosalpinx was uncertain in their second group, which consisted of patients with 'distal occlusion with no or slight distension of one or both tubes.' We decided to exclude this group from our analysis and to include only the two groups where the presence or absence of hydrosalpinx was clear. In using the series of Fleming and Hull (1996), we combined the group of patients with tubal infertility without hydrosalpinx and the group of surgically sterilized patients to form the control group. For the series of De Witt *et al*. (1997), we combined the group of hydrosalpinges visible on ultrasound and the group of hydrosalpinges not visible on ultrasound but seen on hysterosalpingography or laparoscopy.

In these series, there were no other associated infertility factors. The general characteristics of the various populations studied were similar. The patients were <40 years old, except those of Strandell *et al*. (1994), who did not indicate age, and those of Blazar *et al*. (1997), who included patients from 24 to 44 years of age. Only Wainer *et al*. (1997) reported the total duration of infertility and its type (primary or secondary), and the distribution was similar between the two groups. Fleming and Hull (1996), De Witt *et al*. (1997) and Ng and Ho (1997) specified that it involved the first IVF cycle. Only Fleming and Hull (1996) specified the IVF cycle and the duration of infertility. The characteristics of the spermatozoa were normal as defined by the World Health Organization.

Frozen embryos were not excluded from our analysis. We combined the groups with and without frozen embryos from Strandell *et al*. (1994). Only one series reported the frozen embryo transfers as a percentage of total embryo transfers (Sims *et al*., 1993). Akman *et al*. (1996) included only frozen embryos. The six other series were not specific in this regard.

The stimulation protocols varied substantially according to centre but did not appear to differ between the two groups being compared in five series. The number of oocytes retrieved, the number of embryos obtained, and the number of embryo transfers were similar between the two groups in all but one of the series included in the study. Blazar *et al*. (1997) found these indicators higher in the hydrosalpinx group.

Outcome measures

Four outcome measures were evaluated from each study. (i) Pregnancy rate: number of pregnancies achieved per number of embryos transferred. The diagnosis of pregnancy was made with ultrasound in nine of the 13 studies. Extrauterine pregnancies were included in the number of pregnancies. Andersen *et al*. (1994) diagnosed pregnancy when the β-human chorionic gonadotrophin (βHCG) assay was positive; we excluded those biochemical pregnancies in our calculation of the number of ultrasound pregnancies. Sharara *et al*. (1996) calculated the number of ongoing pregnancies by subtracting the early fetal losses from the first trimester. De Witt *et al*. (1997) diagnosed pregnancy when the βHCG was positive, and ongoing pregnancy when fetal heart beat was observed on ultrasound examination. (ii) Implantation rate: number of developing gestational sacs observed upon ultrasound divided by the number of embryos transferred. These data were not always available from the published articles, and remained unavailable for three of the studies even after correspondence with the authors (Sims *et al*., 1993; Strandell *et al*., 1994; Murray *et al*., 1996). (iii) Delivery rate: number of live deliveries per transfer. Sharara *et al*. (1996) obtained the delivery rate by subtracting the multiple gestation rate from the pregnancy rate. The delivery rate could not be calculated in the series of De Witt *et al*. (1997). (iv) Early pregnancy loss, which included ectopic pregnancies, biochemical pregnancies, and early spontaneous abortion. Not all of the studies included all of these parameters. When the number of biochemical pregnancies was specified in the two groups, it was included in the analysis (Andersen *et al*., 1994; Blazar *et al*., 1997). The upper limit of gestational age used to define the term 'early pregnancy loss' varied among the studies: 12 weeks for Andersen *et al*. (1994), 15 weeks for Sharara *et al*. (1996), Blazar *et al*. (1997) and Wainer *et al*. (1997); 20 weeks for Sims *et al*. (1993), Van Dromme *et al*. (1995), Akman *et al*. (1996), Katz *et al*. (1996) and Barmat *et al*. (1997); and 22 weeks for Strandell *et al*. (1994). Murray *et al*. (1996), Fleming and Hull (1996), Ng and Ho (1997) and De Witt *et al*. (1997) did not clarify their use of this term.

Statisitics

The Mantel–Haenszel (1959) statistical method was used in the meta-analysis to calculate the effect of the presence of a hydrosalpinx (Greenland and Salvan, 1990). The results are presented as odds ratios (OR) with their 95% confidence intervals (CI) for each outcome measure. The overall OR was calculated for each outcome measure. The statistical validity of the overall odds ratio was calculated using the χ^2-test for homogeneity (Dersimonian and Laird, 1986).

Results

This meta-analysis confirmed that pregnancy rates are significantly lower in the presence of hydrosalpinx. The rate was 31.2% for the tubal sterility group without hydrosalpinx and 19.67% for the group with hydrosalpinx (OR: 0.64; 95% CI: 0.56, 0.74) (Table II). The results were homogeneous, with the same trend in all studies. The implantation rate in the hydrosalpinx group was only slightly more than half that of the non-hydrosalpinx group, at 8.53 and 13.68% respectively (OR: 0.63; 95% CI: 0.55, 0.72) (Table III). This difference in implantation rates was calculated from a total of 21 576 embryo transfers compiled for this meta-analysis. All of the series included had similar results for this measure as well. Similarly, the delivery rate per transfer in the hydrosalpinx group was only slightly more than half that of the non-hydrosalpinx group, 13.4 and 23.4% respectively (OR: 0.58; 95% CI: 0.49, 0.69) (Table IV). This rate was necessarily lower, since it is directly related to the implantation rate and the number of early pregnancy losses. The incidence of early pregnancy loss was higher in the hydrosalpinx group (43.65%) than in the control group (31.11%) (OR: 1.78; 95% CI: 1.31, 2.41) (Table V). Some studies showed an inverse tendency for this measure, which did not reach statistical significance (Van Dromme *et al*., 1995; Akman *et al*., 1996; De Witt *et al*., 1997; Ng and Ho, 1997; Wainer *et al*., 1997). The χ^2-test for heterogeneity was significant for the pregnancy rate (29.2 with 14 df) and the delivery rate (23.13 with 13 df). The meta-analysis data are summarized in Table VI.

Discussion

A meta-analysis differs from a simple review of the literature by its exhaustive nature and rigorous qualitative and quantitative methodological approaches. In terms of statistical methodology, we did not use the Mantel–Haenszel–Peto method described by Yusuf *et al*. (1985) because of the potential bias in the value of the exact OR when it is not close to one.

Bias in a meta-analysis usually involves the general characteristics of the populations or the selection criteria. All of the series included in our study had homogeneous populations and the selection criteria for each group were identical. However, none of the series gave information regarding associated diseases, such as genital malformations, endometriosis, infections or infectious sequelae. Only Fleming and Hull (1996) specified the IVF cycle and the duration of infertility.

Publication bias generally occurs because studies that find no significant differences between the groups are less likely to be published. It is difficult to control for such bias (Dickersin and Berlin, 1992), but we tried to limit it by actively pursuing data from series available only in abstract form and by writing to numerous authors to complete the missing data.

The basic source of selection bias in these studies is related to the uncertainty of hydrosalpinx diagnoses. Hydrosalpinx is defined as a distal tubal obstruction associated with tubal dilatation due to fluid accumulation. When the diagnosis is established solely by hysterosalpingography, there may be numerous false positives due to some 'flat tube' obstructions that may be artificially and transiently dilated on the hysterosalpingogram. The permanence of the dilatation and the volume of the hydrosalpinx are better appreciated using endovaginal ultrasound (De Witt *et al*., 1997). A drained hydrosalpinx, however, may not be seen on ultrasound and can thus lead to false negative results. This diagnostic and prognostic uncertainty regarding hydrosalpinx extends to the mucosa and tubal walls as well, and it was impossible for us to determine which

Table II. Pregnancy rates

First author and year of publication	Hydrosalpinx group No. (%)	Group without hydrosalpinx No. (%)	Odds ratio (95% CI)
Andersen[a] (1994)	9/91 (9.8)	224/744 (30.1)	0.25 (0.13–0.52)[b]
Strandell (1994)	14/121 (11.57)	89/367 (24.25)	0.41 (0.22–0.75)[b]
Sims (1993)	43/234 (18.37)	341/1287 (26.49)	0.62 (0.44–0.89)[b]
Blazar[a] (1995)	39/161 (24.22)	116/385 (30.13)	0.74 (0.44–1.13)
Van Dromme (1995)	7/69 (10.14)	14/61 (22.95)	0.38 (0.14–1.01)
Sharara (1996)	27/103 (26.21)	30/89 (33.70)	0.70 (0.38–1.30)
Akman (1996)	1/14(7.1)	24/98 (24.5)	0.24 (0.03–1.91)
Murray (1996)	8/45 (17.77)	57/141 (40.42)	0.32 (0.14–0.73)[b]
Katz (1996)	16/95 (16.84)	467/1268 (36.82)	0.35 (0.20–0.60)[b]
Fleming (1996)	18/77 (23.37)	63/212 (29.71)	0.72 (0.39–1.32)
Wainer[a] (1997)	49/267 (18.35)	199/867 (22.95)	0.75 (0.53–1.07)
Barmat[a] (1997)	42/106 (39.62)	502/1150 (43.65)	0.85 (0.56–1.27)
Ng[a] (1997)	9/41 (21.95)	11/92 (11.96)	2.07 (0.78–5.47)
De Witt[a] (1997)	41/224 (18.3)	66/326 (20.25)	0.88 (0.57–1.36)
Total	323/1642 (19.67%)	2203/7061 (31.2%)	0.64 (0.56–0.74)[b]

[a]Excluding biochemical pregnancies.
[b]Odds ratio significantly different from 1 ($P < 0.05$).
χ^2-test for heterogeneity (with 13 df) = 29.2 ($P < 0.05$).
CI = confidence interval.

Table III. Implantation rates

First author and year of publication	Hydrosalpinx group No. (%)	Group without hydrosalpinx No. (%)	Odds ratio (95% CI)
Andersen (1994)	8/273 (2.93)	221/2152 (10.26)	0.26 (0.13–0.54)[a]
Strandell (1994)	–	–	[b]
Sims (1993)	–	–	[b]
Blazar (1995)	56/656 (8.53)	161/1435 (11.22)	0.74 (0.54–1.02)
Van Dromme (1995)	8/190 (4.21)	17/154 (11.04)	0.35 (0.15–0.84)[a]
Sharara (1996)	43/437 (9.84)	50/396 (12.62)	0.76 (0.49–1.16)
Akman (1996)	2/40 (5.0)	30/289 (10.4)	0.45 (0.10–1.98)[b]
Murray (1996)	–	–	
Katz (1996)	17/434 (3.91)	643/5577 (11.53)	0.31 (0.19–0.51)[a]
Fleming (1996)	19/218 (8.71)	94/599 (15.70)	0.51 (0.31–0.86)[a]
Wainer (1997)	58/717 (8.09)	272/2231 (12.19)	0.63 (0.47–0.85)[a]
Barmat (1997)	55/352 (15.63)	795/3795 (20.95)	0.7 (0.54–0.94)[a]
Ng (1997)	9/117 (7.7)	20/263 (7.6)	1.01 (0.45–2.30)
DeWitt (1997)	60/495 (12.12)	11/756 (14.68)	0.80 (0.57–1.12)
Total	335/3929 (8.53%)	2414/17647 (13.68%)	0.63 (0.55–0.72)[a]

[a]Odds ratio significantly different from 1 ($P < 0.05$).
[b]Exact odds ratio could not be calculated.
χ^2-test for heterogeneity (with 10 df) = 19.60 (not significant).
CI = confidence interval.

patients in these series might have benefited from surgical treatment.

The frozen embryos may also have induced selection bias. Strandell *et al*. (1994), with a very small sample of frozen embryos, found pregnancy rates similar to those with fresh embryos.

Outcome bias may thus have been present in terms of the presence or absence of hydrosalpinx and the definition of pregnancy and of fetal loss. The diagnostic method was the same for both groups in every study, however.

The χ^2-test for heterogeneity was significant for the pregnancy rate (with 14 df) and for the delivery rate (with 13 df): this is related to the heterogeneity of some series, all with limited numbers of patients. The series of Ng and Ho (1997) is the only one to show an inverse trend for the pregnancy rate, the implantation rate, and the delivery rate. It included only the first IVF attempt and involved a small number of patients.

Various pathophysiological hypotheses might explain the lower pregnancy rates in the presence of hydrosalpinx. A permanent communication between the tube and the uterine cavity allows the passage of tubal fluid towards the cavity (Mansour *et al*., 1991). The flow of the liquid may hinder the implantation of the egg by purely mechanical means, by 'washing' the uterine cavity. Andersen emphasizes the frequency of reported episodes of hydrorrhoea and of fluid accumulation in the uterine cavity during the second half of the menstrual cycle in the most severe cases (Andersen *et al*., 1996)

Hydrosalpinx fluid contains lower levels of proteins and bicarbonate than does serum and may also contain cellular or infectious debris, lymphocytes, and other components, which

Table IV. Delivery rates per transfer

First author and year of publication	Hydrosalpinx group No. (%)	Group without hydrosalpinx No. (%)	Odds ratio (95% CI)
Andersen (1994)	6/91 (6.59)	170/744 (22.85)	0.24 (0.10–0.56)[a]
Strandell (1994)	8/121 (6.61)	63/367 (17.16)	0.34 (0.16–0.74)[a]
Sims (1996)	23/234 (9.83)	244/1287 (18.96)	0.46 (0.30–0.73)[a]
Blazar (1995)	29/161 (18.01)	91/385 (23.63)	0.71 (0.45–1.13)
Van Dromme (1995)	7/69 (10.14)	13/61 (21.31)	0.42 (0.15–1.13)
Sharara (1996)	19/101 (18.81)	18/89 (20.22)	0.91 (0.45–1.86)
Akman (1996)	1/14 (7.14)	19/98 (17.38)	0.32 (0.04–2.60)
Murray (1996)	4/45 (8.89)	43/141 (30.49)	0.22 (0.07–0.66)[a]
Katz (1996)	9/95 (9.47)	321/1268 (25.31)	0.31 (0.15–0.62)[a]
Fleming (1996)	13/77 (16.88)	54/212 (25.47)	0.59 (0.30–1.16)
Wainer (1997)	38/267 (14.23)	150/867 (17.30)	0.79 (0.54–1.17)
Barmat (1997)	28/106 (26.4)	387/1150 (33.65)	0.71 (0.45–1.11)
Ng (1997)	5/41 (12.2)	6/92 (6.5)	1.99 (0.57–6.94)[b]
DeWitt (1997)	–	–	
Total	190/1418 (13.4%)	1579/6735 (23.44%)	0.58 (0.49–0.69)[a]

[a]Odds ratio significantly different from 1 ($P < 0.05$).
[b]Including biochemical pregnancies.
χ^2-test for heterogeneity (with 13 df) = 23.13 ($P < 0.05$).
CI = confidence interval.

Table V. Early pregnancy losses

First author and year of publication	Hydrosalpinx group No. (%)	Group without hydrosalpinx No. (%)	Odds ratio (95% CI)
Andersen (1994)[a]	14/20 (70)	95/265 (35.86)	3.61 (1.39–9.37)[b]
Strandel l(1994)	6/14 (42.85)	26/89 (29.21)	1.82 (0.57–5.76)
Sims (1996)	20/43 (46.51)	97/341 (28.44)	2.19 (1.15–4.16)[b]
Blazar[a] (1995)	16/45 (35.55)	41/132 (31.06)	1.22 (0.60–2.50)
Van Dromme (1995)	0/7 (0)	1/14 (7.14)	0.19 (0.00–131.8)
Sharara (1996)	13/27 (48.15)	8/30 (26.66)	2.55 (0.84–7.72)
Akman (1996)	0/1 (0)	5/24 (20.8)	0.04 (0.00–10^7)
Murray (1996)	4/8 (50)	13/57 (22.80)	3.38 (0.74–15.4)
Katz (1996)	7/16 (43.75)	144/467 (30.83)	1.74 (0.64–4.78)
Fleming (1996)	5/18 (27.77)	9/63 (14.28)	2.31 (0.66–8.05)
Wainer (1997)	10/49 (20.41)	47/199 (23.61)	0.83 (0.38–1.79)
Barmat (1997)	36/64 (56.25)	195/582 (33.5)	2.55 (1.5–4.3)[b]
Ng (1997)	4/9 (44.4)	5/11 (45.45)	0.96 (0.16–5.64)
DeWitt (1997)	24/41 (58.53)	47/66 (71.2)	0.57 (0.25–1.29)
Total	158/362 (43.65%)	728/2340 (31.11%)	1.72 (1.34–2.20)[b]

[a]Including biochemical pregnancies.
[b]Odds ratio significantly different from 1 ($P < 0.05$).
χ^2-test for heterogeneity (with 13 df) = 19.7 (not significant).
CI = confidence interval.

Table VI. Meta-analysis

Outcome criteria	Group with hydrosalpinx (%)	Group without hydrosalpinx (%)	Odds ratio	Confidence interval
Pregnancy rate	19.67	31.2	0.64	0.56–0.74[a]
Implantation rate	8.53	13.68	0.63	0.55–0.72[a]
Delivery rate	13.4	23.44	0.58	0.49–0.69[a]
Early pregnancy loss rate	43.65	31.11	1.72	1.34–2.20[a]

[a]Odds ratio significantly different from 1 ($P < 0.05$).

may include cytokines, prostaglandins, leukotrienes and catecholamines, all of which may have deleterious inflammatory, infectious, or immunological effects. These components may cause changes in oocytes during the retrieval phase or have deleterious effects on the embryo or endometrium, because of their movement, not only within the tubes but also in lymphatic or vascular channels (David *et al*., 1969; Owman *et al*., 1992). Several experiments have shown early inhibition of embryonic development in mouse embryos exposed to human hydrosalpinx fluid in various dilutions (Mukerjee *et al*., 1996; Rawe *et al*., 1997; Sachdev *et al*., 1997). The toxic effect of this fluid is found even in weak concentrations. Recently, it has been shown that the composition and the amount of hydrosalpinx fluid can adversely affect the endometrium by lowering levels of certain mediators necessary for embryonic implantation. Lessey *et al*. (1994, 1995, 1996) observed this effect with certain integrins. Meyer *et al*. (1997) obtained similar results, finding that some integrins were again expressed after surgical removal of the tubal fluid.

Most studies do not distinguish between unilateral and bilateral hydrosalpinx. When this distinction is made (Wainer

et al., 1997), however, the pregnancy and implantation rates are significantly lower among patients with bilateral hydrosalpinx. The harmful effect of hydrosalpinx on the development of a pregnancy after IVF may thus have a threshold effect, and this threshold of toxicity may be reached much more frequently in cases of bilateral disease. The same reasoning may apply to small and large hydrosalpinges: the latter are more likely to be visible on ultrasonography (De Witt *et al*., 1998).

Moreover, hydrosalpinges may also resemble large follicles and cause false interpretations during ovarian stimulation monitoring. They may also be inadvertently punctured during oocyte retrieval; infectious or toxic agents might thus jeopardize the quality of the oocytes retrieved or even contaminate the culture media.

This meta-analysis, although based on the results of retrospective studies, demonstrates that hydrosalpinx present during IVF–embryo transfer has negative consequences on the pregnancy rate, the implantation rate, the live delivery rate per transfer, and the rate of early pregnancy loss. It would be premature, however, to conclude that routine salpingectomy should be performed on all hydrosalpinges, before results are available from the randomized, prospective studies that are currently in progress. In their article subtitled 'Blind victimization of the Fallopian tube', Puttemans and Brosens (1996) recently proposed selective triage of patients presenting with hydrosalpinx. Only a randomized study comparing a group of patients with hydrosalpinx to a group that has undergone salpingectomy or the placement of a proximal tubal clip can definitively answer this question about the benefit of surgical treatment.

References

Akman, M.A., Garcia, J.E., Danewood, M.D. *et al*. (1996) Hydrosalpinx affects the implantation of previously cryopreserved embryos. *Hum. Reprod*., **11,** 1013–1014.

Andersen, A.N., Lindhard, A., Loft, A. *et al*. (1996) The infertile patient with hydrosalpinges—IVF with or without salpingectomy? *Hum. Reprod*., **11,** 2081–2084.

Andersen, A.N., Yue, Z., Meng, F.J. and Petersen, K. (1994) Low implantation rate after in-vitro fertilization in patients with hydrosalpinges diagnosed by ultrasonography. *Hum. Reprod*., **9,** 1935–1938.

Barmat, L., Rauch, A., Kowalik, A. *et al*. (1997) The effect of hydrosalpinx on IVF–ET outcome. (Abstr.). Presented at Xth World Congress on IVF, Vancouver, May 1997. *J. Assist. Reprod. Genet*. **14,** (Abstract book), 205S, PP20–442.

Blazar, A.S., Hogan, J.W., Seifer, D.B. *et al*. (1997) The impact of hydrosalpinx on successful pregnancy in tubal factor infertility treated by in-vitro fertilization. *Fertil. Steril*., **67,** 517–520.

Claman, P., Morisson, M. Toye, B. *et al*. (1997) The presence of hydrosalpinx does not affect pregnancy rates with IVF–ET. Presented at Xth World Congress on IVF, Vancouver, May, 1997. *J. Assist. Reprod. Genet*. **14,** (Abstract book), 208S, PP20–453.

David, A., Garcia, C.R. and Czernobilsky, B. (1969) Human hydrosalpinx. *Am. J. Obstet. Gynecol*., **105,** 400–411.

Dechaud, H., Arnal, F., Humeau, C. *et al*. (1995) Tubal infertility: IVF results after bilateral salpingectomy versus without salpingectomy (prospective randomized study). *Contracept. Fertil. Sex*., **23** (Suppl. 9), special no. 1.

Dersimonian, R. and Laird, N. (1986) Combining evidence in clinical trials. *Controlled Clin. Trials*, **7,** 177–188.

De Witt, W., Gowrising, C.J., Kuik, D.J. *et al*. (1997) Only hydrosalpinges visible on ultrasound are associated with reduced implantation and pregnancy rates after IVF. (Abstr.) *Hum. Reprod*., **12** (Abstract book 1), 170, P-105.

Dickersin, K. and Berlin, J.A. (1992) Meta-analysis: state-of-the-science. *Epidemiol. Rev.*, **14,** 154–176.

Fleming, C. and Hull, M.G. (1996) Impaired implantation after in-vitro fertilization treatment associated with hydrosalpinx. *Br. J. Obstet. Gynaecol*., **103,** 268–272.

Freeman, M.R., Whitworth, C.M. and Hill, G.A. (1995) Hydrosalpinx reduces *in vitro* fertilization-embryo transfer implantation rates and *in vitro* blastocyst development. (Abstr.) *The 51st Annual Meeting of the American Society for Reproductive Medicine, Seattle, USA*, (Abstract book), p. 259.

Fukui, A. Fujii, S. and Saito, Y. (1997) The influences of the persistent existence of hydrosalpinx on IVF outcome. Presented at Xth World Congress on IVF, Vancouver, May, 1997. *J. Assist. Reprod. Genet*., **14,** (Abstract book), 209S, PP20–457.

Greenland, S. and Salvan, A. (1990) Bias in the one-step (Peto) method for pooling study results. *Stat. Med*., **9,** 247–252.

Kassabji, M., Sims, J.A., Butler, L. and Muasher, S.J. (1994) Reduced pregnancy outcome in patients with unilateral or bilateral hydrosalpinx after *in vitro* fertilization. *Eur. J. Obstet. Gynecol. Reprod. Biol*., **56,** 129–132.

Katz, E., Akman, M.A., Damewood, M.D. and Garcia, J.E. (1996) Deleterious effect of the presence of hydrosalpinx on implantation and pregnancy rates with in-vitro fertilization. *Fertil. Steril*., **66,** 122–125.

Lessey, B.A., Castelbaum, A.J., Riben, M. *et al*. (1994) Effect of hydrosalpinges on markers of uterine receptivity and success in IVF. (Abstr.) *The 50th Annual Meeting of the American Society for Reproductive Medicine, San Antonio, TX, USA*, (Abstract book), p. 45.

Lessey, B.A., Castelbaum, A.J., Sawin, S.W. and Sun, J. (1995) Integrins as markers of uterine receptivity in women with primary unexplained infertility. *Fertil. Steril*., **63,** 553–542.

Lessey, B.A., Yeh, I., Castelbaum, A.J. *et al*. (1996) Endometrial progesterone receptors and markers of uterine receptivity in the window of implantation. *Fertil. Steril*., **65,** 477–483.

Mansour, R.T., Aboulghar, M.A., Serour, G.I. and Riad, R. (1991) Fluid accumulation of the uterine cavity before embryo transfer: a possible hindrance for implantation. *J. In Vitro Fertil. Embryo Transfer*, **8,** 157–159.

Mantel, N. and Haenszel, W. (1959) Statistical aspects of the analysis of data from retrospective studies of disease. *J. Natl Cancer Inst*., **22,** 719–748.

Meyer, W.R., Castelbaum, A.J., Somkuti, S. *et al*. (1997) Hydrosalpinges adversely affect markers of endometrial receptivity. *Hum. Reprod*., **12,** 1393–1398.

Mukerjee, T., Copperman, A.B., McCaffrey, C. *et al*. (1996) Hydrosalpinx fluid has embryotoxic effects on murine embryogenesis: a case for prophylactic salpingectomy. *Fertil. Steril*., **66,** 851–853.

Murray, D.L., Sagoskin, A.W., Hall, J.L. and Levy, M.J. (1996) The effect of hydrosalpinges in IVF pregnancy rates. (Abstr.) *The American Society for Reproductive Medicine 52nd Annual Meeting*. American Fertility Society, program supplement, S222.

Ng, E.H.Y. and Ho, P.C. (1997) Hydrosalpinx may not impair the success of IVF treatement. (Abstr.) Presented at the 13th ESHRE Annual Meeting, Edinburgh, June 1997. *Hum. Reprod*., **12** (Abstract book 1), 144, P-051.

Owman, C., Kannisto, P. and Liedberg, F. (1992) In Sjoberg, N.O., Hamberger, L. and Janson, P.O. (eds) *Local Regulation of Ovarian Function*. Parthenon, Carnforth, Lancs, UK, pp. 149–170.

Puttemans, P.J. and Brosens, I.A. (1996) Preventive salpingectomy of hydrosalpinx prior to IVF. Salpingectomy improves in-vitro fertilization outcome in patient with a hydrosalpinx: blind victimization of the Fallopian tube? *Hum. Reprod*., **11,** 2079–2081.

Rawe, V.J., Compton, M.G., Liu, J. *et al*. (1997) Effect of human hydrosalpinx on murine embryo development and implantation. *Fertil. Steril*., **68,** 668–670.

Sachdev, R., Kemmann, E., Bohrer, M.K. and El-Danasouri, I. (1997) Detrimental effect of hydrosalpinx fluid on the development and blastulation of mouse embryos *in vitro*. *Fertil. Steril*., **68,** 531–533.

Sharara, F.I., Scott, R.T., Marut, E.L. and Queenan, J.T. (1996) In-vitro fertilization outcome in women with hydrosalpinx. *Hum. Reprod*., **11,** 526–530.

Shelton, K.E., Butler, L., Toner, J.P. *et al*. (1996) Salpingectomy improves the pregnancy rate in in-vitro fertilization patients with hydrosalpinx. *Hum. Reprod*., **11,** 523–525.

Sims, J.A., Jones, D., Butler, L. and Muasher, S.J. (1993) Effect of hydrosalpinx in in-vitro fertilization. (Abstr.) *The American Society for Reproductive Medicine 49th Annual Meeting*. American Fertility Society, program supplement, S95.

Strandell, A., Waldenstrom, U., Nillson, L. and Hamberger, L. (1994) Hydrosalpinx reduces in-vitro fertilization/embryo transfer pregnancy rates. *Hum. Reprod*., **9,** 861–863.

Van Dromme, J., Chasse, E., Lejeune, B. *et al*. (1995) Hydrosalpinges in in-vitro fertilization: an unfavourable prognostic feature. *Hum. Reprod*., **10,** 576–579.

Wainer, R., Camus, E., Camier, B. *et al*. (1997) Does hydrosalpinx reduce the pregnancy rate following *in vitro* fertilization. *Fertil. Steril*., **68,** 1022–1026.

Yusuf, S., Peto, R., Lewis, J. *et al*. (1985) Beta blockade during and after myocardial infarction: an overview of the randomized trials. *Prog. Cardiovasc. Dis*., **27,** 335–371.

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