

Table 1. Available studies on the relation between endometriosis and miscarriage (1995-2015).

Study (citation)	Country	Study period	Study design	Sample size ^a	Main finding ^b	Main limitations
Matoras <i>et al.</i> , 1998 (10)	Spain	n.r.	Prospective nested cohort study	62	RR=1.3 (0.5-3.4)	Small sample size, unadjusted for age and mode of conception
Omland <i>et al.</i> , 2005 (11)	Norway	1990-2002	Retrospective cohort of IVF pregnancies	212	OR=2.0 (1.2-3.1)	Adjusted but not matched for age. Include multiple pregnancies
Gergolet <i>et al.</i> , 2010 (12)	Italy-Slovenia	2000-2008	Retrospective cohort of women operated for uterine septum	20	OR=2.7 (0.7-10.1)	Small sample size, selected population (operated uterine septum), unadjusted for age
Benaglia <i>et al.</i> , 2012 (13)	Italy-Spain	2005-2009	Retrospective, nested cohort on IVF pregnancies	78	OR=1.1 (0.5-1.4)	Not designed for miscarriage, small sample size, unadjusted for age.
Hjordt Hansen <i>et al.</i> , 2014 (14)	Denmark	1977-2009	Retrospective cohort with national registers	25,834	RR=1.2 (1.2-1.3) for natural / RR=4.3 (3.4-5.5) for ART	Age matched at study entry but not at age of pregnancy.
Mekaru <i>et al.</i> , 2014 (15)	Japan	1995-2011	Retrospective cohort of women who underwent laparoscopy	49	OR=1.0 (0.4-2.6)	Small sample size, unadjusted for age
Aris, 2014 (16)	Canada	1997-2008	Retrospective cohort with national registers	784	OR=1.9 (1.2-2.9)	Unadjusted for age and mode of conception, underestimation of the rate of miscarriage.

^a Refers to the number of women with endometriosis.

^b Data in parenthesis are 95%CI

Table 2. Baseline characteristics of the two study groups.

Characteristics	Endometriosis n=313	Controls n=313	p
Age (years)	35.5 ± 3.5	35.5 ± 3.5	0.95
BMI (Kg/m ²)	21.6 ± 3.1	22.2 ± 3.7	0.04
Previous deliveries	32 (10%)	47 (15%)	0.09
Previous miscarriages			0.43
None	270 (86%)	255 (82%)	
1	34 (11%)	45 (14%)	
≥ 2	9 (3%)	13 (4%)	
Duration of infertility (years)	3.5 ± 2.0	4.1 ± 2.5	0.004
Previous IVF cycles			0.14
None	117 (38%)	148 (47%)	
1	112 (36%)	97 (31%)	
≥ 2	84 (26%)	68 (22%)	
Day 3 serum FSH (IU/ml)	7.6 ± 3.0	7.6 ± 2.9	0.93
AMH (ng/ml)	1.7 (0.9-3.3)	1.9 (0.9-3.6)	0.31
Intramural fibroids	29 (9%)	31 (10%)	0.79
Indication to IVF			<0.001
Endometriosis	205 (66%)	0 (0%)	
Endometriosis + male factor	108 (34%)	0 (0%)	
Male factor	0 (0%)	155 (49%)	
Tubal factor	0 (0%)	27 (9%)	
Unexplained	0 (0%)	118 (38%)	
Mixed (without endometriosis)	0 (0%)	13 (4%)	

Data is presented as Mean ± SD, Median (Interquartile Range-IQR) or Number (%).

Supplementary Table 1. Main endometriosis-related characteristics of the affected women (n=313).

Characteristics	Number (%)
<i>History of endometriosis</i>	
Previous interventions for endometriosis	
None	80 (26%)
1	198 (63%)
≥ 2	35 (11%)
Previous excision of ovarian endometriomas	
None	62 (27%)
Unilateral	117 (50%)
Bilateral	54 (23%)
Previous removal of deep peritoneal nodules	98 (42%)
<i>Endometriosis at the time of IVF (sonographic findings)</i>	
Ovarian endometriomas	
None	154 (49%)
Unilateral	134 (43%)
Bilateral	25 (8%)
Deep peritoneal nodules	17 (5%)
Adenomyosis	29 (9%)

Supplementary Table 2. Characteristics of the fresh cycles in the two study groups.

Characteristics	Endometriosis n=235	Controls n=235	P
Regimen of ovarian hyper-stimulation			0.10
Long protocol	112 (48%)	94 (40%)	
Flare-up protocol	37 (16%)	31 (13%)	
GnRH antagonists	82 (35%)	109 (46%)	
Others	4 (2%)	1 (1%)	
Duration of stimulation (days)	10.1 ± 2.2	10.2 ± 2.4	0.52
Total dose of FSH administered (IU)	2,732 ± 1,330	2,464 ± 1,194	0.02
Estradiol at the time of hCG administration (pg/ml)	1,934 ± 925	1,886 ± 862	0.58
Total number of oocytes retrieved	7.1 ± 4.0	8.0 ± 4.2	0.03
In vitro fertilization technique used			0.46
IVF	42 (18%)	35 (15%)	
ICSI	193 (82%)	200 (85%)	
Stage at embryo transfer			0.56
48 hours	70 (30%)	61 (26%)	
72 hours	133 (57%)	136 (58%)	
Blastocysts	32 (13%)	38 (16%)	
Number of embryos-blastocysts transferred			0.28
1	65 (28%)	71 (30%)	
2	152 (65%)	154 (66%)	
3	18 (7%)	10 (4%)	

Data is presented as Mean ± SD or Number (%).

Supplementary Table 3. Characteristics of the frozen cycles in the two study groups.

Characteristics	Endometriosis n=78	Controls n=78	p
Protocol			0.98
Frozen eggs, HRT	17 (22%)	17 (22%)	
Frozen embryos, HRT	30 (38%)	29 (37%)	
Frozen Embryos, natural cycle	31 (40%)	32 (41%)	
In vitro fertilization technique used			0.02
IVF	16 (20%)	5 (6%)	
ICSI	62 (80%)	73 (94%)	
Stage at embryo transfer			0.86
48 hours	6 (8%)	6 (8%)	
72 hours	23 (29%)	20 (25%)	
Blastocysts	49 (63%)	52 (67%)	
Number of embryos-blastocysts transferred			0.88
1	49 (63%)	52 (67%)	
2	28 (36%)	25 (32%)	
3	1 (1%)	1 (1%)	

HRT: Hormone replacement treatment

Table 3. Subgroup analyses on the risk of miscarriage

Subgroup	Endometriosis		Controls		p	Crude OR (95%CI)	Adj. OR (95%CI)
	Total	N. abortion (%)	Total	N. abortion (%)			
Type of cycle							
Fresh cycles	235	32 (14%)	235	42 (18%)	0.25	0.72 (0.44 - 1.20)	0.80 (0.47 - 1.35) ^a
Frozen cycles	78	16 (21%)	78	18 (23%)	0.85	0.86 (0.40 - 1.84)	0.84 (0.37 - 1.93) ^b
Number of embryos transfered							
One	114	15 (13%)	123	20 (16%)	0.58	0.78 (0.38 - 1.61)	0.73 (0.34 - 1.58) ^c
≥ 2	199	33 (17%)	190	40 (21%)	0.30	0.75 (0.45 - 1.24)	0.85 (0.50 - 1.44) ^c
Endometriomas at ultrasound (all cases)							
Yes	159	30 (19%)	159	33 (21%)	0.78	0.89 (0.51 - 1.54)	1.00 (0.56 - 1.81) ^d
No	154	18 (12%)	154	27 (18%)	0.20	0.62 (0.33 - 1.19)	0.63 (0.32 - 1.23) ^d
Endometriomas at ultrasound (fresh cycles)							
Yes	120	20 (17%)	120	27 (21%)	0.62	0.80 (0.42-1.54)	0.92 (0.46-1.84) ^a
No	115	12 (10%)	115	15 (14%)	0.33	0.63 (0.29-1.37)	0.71 (0.31-2.61) ^a
Previous surgery for endometriosis							
Yes	233	32 (14%)	233	41 (18%)	0.31	0.75 (0.45 - 1.23)	0.82 (0.49 - 1.40) ^d
No	80	16 (20%)	80	19 (24%)	0.70	0.80 (0.38 - 1.70)	0.76 (0.34 - 1.68) ^d

^a Model adjusted for BMI, parity, duration of infertility, male factor, total dose of FSH administered and number of oocytes retrieved.

^b Model adjusted for BMI, parity, duration of infertility, male factor and IVF technique.

^c Model adjusted for BMI, parity, duration of infertility, male factor and age.

^d Model adjusted for BMI, parity, duration of infertility and male factor.