Human Reproduction Open, pp. 1–8, 2022
https://doi.org/10.1093/hropen/hoac025

human reproduction open

ORIGINAL ARTICLE

Endometriosis and oocyte quality: an analysis of 13 614 donor oocyte recipient and autologous IVF cycles

Mohan S. Kamath [1,*], Venkatesh Subramanian [2], Belavendra Antonisamy [1], and Sesh Kamal Sunkara [2]

[1]Christian Medical College, Vellore, India [2]Division of Women's Health, Faculty of Life Sciences and Medicine, King's College London, London, UK

*Correspondence address. Department of Reproductive Medicine and Surgery, Christian Medical College, Vellore, Tamil Nadu 632004, India. E-mail: mohankamath@cmcvellore.ac.in https://orcid.org/0000-0002-0316-636X

Submitted on February 12, 2022; resubmitted on May 31, 2022; editorial decision on June 06, 2022

STUDY QUESTION: Does endometriosis affect live birth following donor oocyte recipient versus autologous IVF?

SUMMARY ANSWER: There was no significant difference in the live birth rate (LBR) in women with endometriosis undergoing donor oocyte recipient cycles versus autologous IVF cycles.

WHAT IS KNOWN ALREADY: For infertile women with endometriosis, IVF is often considered as a treatment option. Lower implantation and pregnancy rates have been observed following IVF in women with endometriosis. It has been debated whether the lower pregnancy rate is due to the effect on oocyte quality or the endometrium, thus affecting implantation. To delineate whether endometriosis affects oocyte quality or the endometrium, we planned a study, using a donor oocyte recipient model, where the recipients were women diagnosed with endometriosis and compared their outcomes with women who underwent autologous IVF, who had also been diagnosed with endometriosis.

STUDY DESIGN, SIZE, DURATION: Human Fertilization and Embryology Authority (HFEA) anonymized data from 1996 to 2016 were analyzed. This comprised of a total of 758 donor oocyte recipients, where the recipients were women diagnosed with endometriosis, and 12 856 autologous IVF cycles where the women were diagnosed with endometriosis as the sole cause of infertility.

PARTICIPANTS/MATERIALS, SETTING, METHODS: Data on all women with endometriosis undergoing donor oocyte recipient and autologous IVF cycles were analyzed to compare live birth outcomes. Logistic regression analysis was performed adjusting for number of previous IVF cycles, previous live birth, period of treatment, day of embryo transfer, number of embryos transferred and fresh or frozen embryo transfer cycle.

MAIN RESULTS AND THE ROLE OF CHANCE: There was no significant difference in the LBR in women with endometriosis undergoing donor oocyte recipient fresh embryo transfer cycles compared to women undergoing autologous IVF fresh embryo transfer cycles (31.6% vs 31.0%; odds ratio (OR) 1.03, 99.5% CI 0.79–1.35). After adjusting for confounders, there was no significant difference in LBR in women with endometriosis undergoing donor oocyte recipient fresh embryo transfer cycles versus autologous fresh embryo transfer cycles (adjusted OR (aOR) 1.05, 99.5% CI 0.79–1.41).

There was no significant difference in the LBR in women with endometriosis undergoing donor oocyte recipient frozen embryo transfer cycles compared to women undergoing autologous frozen embryo transfer cycles (19.6% vs 24.0%; OR 0.77, 99.5% CI 0.47–1.25). After adjusting for potential confounders, there was no significant difference in the LBR in women undergoing donor oocyte recipient frozen embryo transfer cycles compared with autologous frozen embryo transfer cycles (aOR 0.85, 99.5% CI 0.51–1.41).

LIMITATIONS, REASONS FOR CAUTION: Although the analysis was adjusted for potential confounders, there was no information on the extent and classification of endometriosis as well as oocyte number. Furthermore, adenomyosis is thought to co-exist in women with endometriosis and may have independent pathophysiological mechanisms affecting fertility, for which there was no information.

WIDER IMPLICATIONS OF THE FINDINGS: The study shows no difference in LBR between donor oocyte recipient cycles in which all recipients had endometriosis compared to autologous IVF cycles in women with endometriosis. Therefore, this study finding suggests that there may be a minimal or no effect of oocyte quality on IVF outcomes in women with endometriosis.

STUDY FUNDING/COMPETING INTEREST(S): No funding was obtained. M.S.K. is an associate editor with *Human Reproduction Open*. He was not involved in the editorial or peer review process for the manuscript.

TRIAL REGISTRATION NUMBER: N/A.

Key words: IVF / autologous / endometriosis / live birth / donor oocyte recipient / oocyte donation

WHAT DOES THIS MEAN FOR PATIENTS?

One in 10 women among the reproductive age group is affected by endometriosis. Many women with endometriosis face difficulty in conceiving and are often advised IVF as a treatment option. It has been reported that the success rate of IVF in women with endometriosis is lower compared to women without endometriosis. The main reasons suggested for lower IVF success in women with endometriosis are the poor egg quality and reduced ability of the uterine lining to attach to the embryo. While some studies have suggested the role of poor egg quality as the main reason for lower IVF success in women with endometriosis, others have suggested the role of reduced ability of the uterine lining attaching to the embryo.

This study investigated the impact of egg quality on the IVF outcome in women with endometriosis by using a donor egg model. We compared women with endometriosis who underwent donor egg cycle with women with endometriosis who underwent IVF using their own eggs. The study did not find any difference in live birth in women with endometriosis who underwent donor egg cycle versus IVF in women using their own eggs. The study findings suggest endometriosis may have little effect on egg quality.

Introduction

Endometriosis is a chronic gynecological condition which affects 1 in 10 women in the reproductive age group (Macer and Taylor, 2012). A substantially higher prevalence of endometriosis, of up to 50%, has been reported in women with infertility (den Hartog *et al.*, 2008; Georgiou *et al.*, 2019). ART is often considered as a treatment option for women with endometriosis and infertility (Dunselman *et al.*, 2014; Georgiou *et al.*, 2019).

There has been much debate as to whether the poorer outcome in women with endometriosis is secondary to impairment of either oocyte quality or endometrial receptivity. A systematic review including 22 studies reported lower implantation and pregnancy rates following ART in women with endometriosis compared to women who had tubal factor infertility (Barnhart *et al.*, 2002). The authors suggested that endometriosis has a negative impact on endometrial receptivity as well as the oocyte quality. Another systematic review that included 27 studies, exploring the association between endometriosis and ART outcomes, reported lower implantation and pregnancy rates in women with severe endometriosis compared to the non-endometriosis group (Harb *et al.*, 2013). A study involving the analysis of the Society of Assisted Reproductive Technology (SART) data reported a lower live birth rate (LBR) following autologous fresh and frozen ART, when endometriosis was associated with other causes of infertility compared to infertility causes without an additional diagnosis of endometriosis (Senapati *et al.*, 2016).

The evidence for endometriosis significantly affecting the LBR compared to other causes of fertility, is further corroborated by data from our previous study showing that the live birth after IVF cycles with fresh and frozen embryo transfers in women with endometriosis was significantly lower compared to male factor infertility (23.7% vs 25.9%; odds ratio (OR) 0.89, 95% CI 0.86 to 0.91) (Sunkara *et al.*, 2021).

However, it is unclear how endometriosis affects ART outcomes, whether it is due to the generation of poorer quality oocytes and resulting embryos or due to the endometriosis negatively impacting on endometrial receptivity (Georgiou *et al.*, 2019; Simon *et al.*, 1994). Studies evaluating endometrial receptivity have reported altered gene expression and aberrant cell signaling pathways seen in the endometrium of women with endometriosis when compared with healthy controls (Wei *et al.*, 2009; Lessey and Kim, 2017; Focarelli *et al.*, 2018). Other studies have suggested poor oocyte and embryo quality as the main reason for the lower implantation rate with endometriosis (Simon *et al.*, 1994; Diaz *et al.*, 2000; Orazov *et al.*, 2019). A recent study evaluated treatment outcomes following transfer of frozen-thawed euploid embryos in women with and without endometriosis and reported no difference in LBR between the two groups (Bishop et al., 2021). They inferred that impaired endometrial receptivity may not be the key factor that causes poorer ART outcomes for women with endometriosis.

We aim to address whether the poorer outcomes with endometriosis are due to the effect on the oocyte quality or endometrial receptivity. We compared treatment outcomes following donor oocyte recipient IVF ± ICSI cycles where the recipient had endometriosis versus autologous IVF ± ICSI in women with endometriosis as a sole cause of infertility.

Materials and methods

This study involves retrospective analysis of the Human Fertilization and Embryology Authority (HFEA) dataset. The HFEA is the government regulator for all assisted conception treatment in the UK and as part of its role, data are prospectively collected and validated for all ART cycles conducted in the UK. As this was a retrospective analysis of anonymized data (https://www.hfea.gov.uk/about-us/our-data/), ethics approval was not necessary. Data were extrapolated between the years 1996 and 2016 for the following two cohorts consisting of

donor oocyte recipient IVF cycles, where the recipient had a diagnosis of endometriosis and a second cohort of all autologous IVF cycles with endometriosis as a sole cause of infertility. This consisted of a total of 758 IVF cycles for donor oocyte recipient and a total of 12 856 IVF cycles for autologous. The two cohorts were evaluated against each other to compare LBR per cycle. We also performed a *post hoc* subgroup analysis to explore any differences in the result due to the different period of treatment (1996–2005 and 2006–2016). Additionally, as a control, we included a cohort of recipient women who underwent treatment for male factor (women without endometriosis) and compared them against donor oocyte recipients with endometriosis. Live birth was defined as delivery of one or more neonates with signs of life at ≥24 weeks gestation. IVF ± ICSI for each cohort was referred as IVF in this article.

Information was obtained for the donor oocyte age group (≤20, 21–25, 26–30, 31–35 years) and women undergoing autologous IVF (<35 years), period of treatment, cause of infertility, previous live birth, day of embryo transfer, number of embryos transferred, IVF or ICSI and fresh or frozen embryo transfer. A subgroup analysis was performed from the data acquired, comparing outcomes for fresh versus frozen embryo transfer cycles.

Statistical analysis

Absolute and relative frequencies with 99.5% CIs were used to interpret each cohort with a primary outcome of LBR per cycle. A decision was made to use 99.5% CIs to facilitate analysis of cycle multiplicity.

Distributions of the two cohorts were characterized and stratified by female age, period of treatment, previous live birth, IVF or ICSI, fresh or frozen embryo transfers, day of embryo transfer and number of embryos transferred. Data on all donor oocyte recipient IVF cycles, where the recipients were women diagnosed with endometriosis and all autologous IVF cycles, where endometriosis was the sole cause of infertility in these women, were analyzed to compare the LBR per cycle.

Adjusted logistic regression analysis was performed to compare the LBR between the two cohorts, accommodating for the following confounding factors: number of previous IVF cycles, previous live birth, IVF or ICSI, period of treatment, day of embryo transfer, number of embryos transferred and fresh or frozen embryo transfer cycles. The confounders identified were already known to affect clinical outcomes or potentially were capable of this. Further subgroup analyses for fresh and frozen embryo transfer cycles were also performed. The statistical package Stata, IC version 16 (StataCorp, College Station, TX, USA) was used to analyze the data and a *P*-value of <0.05 was considered statistically significant.

Results

A total of 1 176 357 IVF cycles were performed during the period 1996–2016 as shown in Fig. 1. For the study purpose, 1 162 743 cycles were excluded for the following reasons: cycles with more than one cause of infertility, cycles other than endometriosis, autologous IVF cycles with women's age more than 34 years, surrogacy cycles, cycles where embryos were developed for reasons other than infertility treatment, cycles with missing information on oocyte source and the lack of information on fresh or frozen treatment. A total of 13 614 donor oocyte recipient and autologous IVF cycles with endometriosis and no other cause of infertility were analyzed. There were 758 donor oocyte recipient cycles and 12 856 autologous IVF cycles for final analysis.

Baseline characteristics for the two cohorts are described in Table I. The majority of the IVF cycles in both the cohorts were performed after 2011. For both the cohorts, the majority of cycles were fresh embryo transfers and day of embryo transfer was <5 days. The mean number of embryos transferred was 1.63 (0.7) for donor oocyte recipient and 1.54 (0.8) in autologous IVF cycles.

Live births following donor oocyte recipient cycles versus autologous IVF cycles

There was no significant difference in LBR in women with endometriosis undergoing donor oocyte recipient cycles compared to women undergoing autologous IVF cycles (28.0% vs 29.8%; OR 0.92, 99.5% CI 0.72 to 1.16). After adjusting for potential confounders (number of previous IVF cycles, previous live birth, period of treatment, day of embryo transfer, number of embryos transferred, fresh and frozen cycle), there was no significant difference in LBR in women undergoing donor oocyte recipient cycles versus autologous IVF cycles (adjusted OR (aOR) 1.0, 99.5% CI 0.78 to 1.28) (Table II and Supplementary Table SI).

The *post hoc* subgroup analysis found no significant difference in LBR in women with endometriosis undergoing donor recipient cycles versus autologous cycles for the treatment period between 1996–2005 (aOR 1.08, 99.5% CI 0.66 to 1.79) and 2006–2016 (aOR 0.96, 99.5% CI 0.72 to 1.28) (Table III).

Live births following donor oocyte recipient fresh embryo transfer cycles versus autologous IVF fresh embryo transfer cycles

There was no significant difference in the LBR in women with endometriosis undergoing donor oocyte recipient fresh embryo transfer cycles compared to women undergoing autologous IVF fresh embryo transfer cycles (31.6% vs 31.0%; OR 1.03, 99.5% CI 0.79 to 1.35). After adjusting for potential confounders (number of previous IVF cycles, previous live birth, period of treatment, day of embryo transfer and number of embryos transferred), there was no significant difference in LBR in women undergoing donor oocyte recipient fresh embryo transfer cycles versus autologous IVF fresh embryo transfer cycles (aOR 1.05, 99.5% CI 0.79 to 1.41) (Table II).

Live births after donor oocyte recipient frozen embryo transfer cycles versus autologous IVF cycles

There was no significant difference in the LBR in women with endometriosis undergoing donor oocyte recipient frozen embryo transfer cycles compared to women undergoing autologous IVF frozen embryo transfer cycles (19.6% vs 24.0%; OR 0.77, 99.5% CI 0.47 to 1.25). After adjusting for potential confounders, there was no significant difference in the LBR in women undergoing donor oocyte recipient frozen embryo transfer cycles compared with autologous IVF frozen embryo transfer cycles (aOR 0.85, 99.5% CI 0.51 to 1.41) (Table II).

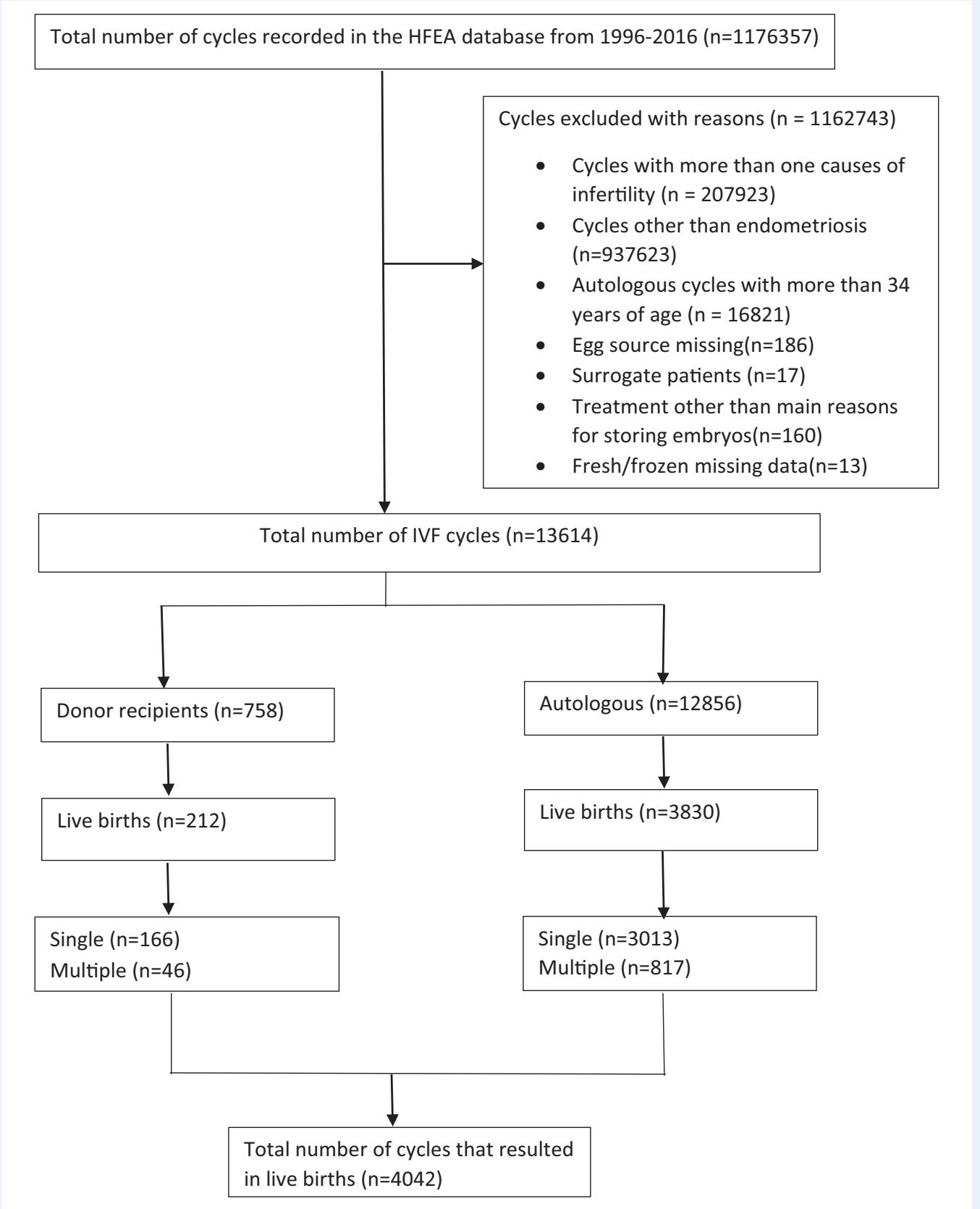

Figure 1. **Data selection process.**

Table I Baseline characteristics of donor oocyte recipient and autologous ART cycles in women with endometriosis (n = 13 614).

Characteristics	Donor (n = 758) n (%)	Autologous IVF cycles (n = 12 856) n (%)	*P*-value
Donor and female age at treatment			
≤20 years	7 (0.9)	12 856* (100.0)	
21–25 years	122 (16.1)		–
26–30 years	216 (28.5)		
31–35 years	324 (42.8)		
Not known	89 (11.7)		
Year of treatment			
1996–2000	68 (8.9)	1422 (11.1)	
2001–2005	134 (17.7)	2649 (20.6)	
2006–2011	200 (26.4)	4150 (32.3)	<0.001
2012–2016	356 (47.0)	4635 (36.0)	
Number of previous IVF cycles			
0	129 (17.0)	6782 (52.7)	
1	154 (20.3)	3388 (26.4)	
2	154 (20.3)	1517 (11.8)	<0.001
3	120 (15.8)	641 (5.0)	
4+	201 (26.5)	528 (4.1)	
Previous live births (yes)	111 (14.6)	1589 (12.4)	0.001
Embryos transferred, mean (SD)	1.63 (0.7)	1.54 (0.8)	0.001
Day of embryo transfer			
<Day 5	545 (71.9)	8874 (69.0)	
≥Day 5	162 (21.4)	2455 (19.1)	0.001
Unknown	51 (6.7)	1527 (11.9)	
Embryo transfer			
Fresh embryo transfer	528 (69.7)	10 628 (82.6)	<0.001
Frozen embryo transfer	230 (30.3)	2228 (17.3)	

*All are under 35 years of age and exact age is not available in the database.

Table II Live birth rate in women with endometriosis following donor oocyte recipient versus autologous ART cycles.

	Donor oocyte recipient cycle	Autologous ART cycle	Unadjusted OR (99.5% CI)	Adjusted OR (99.5% CI)*
Fresh and frozen LBR per cycle	212/758 (28.0%)	3830/12 856 (29.8%)	0.92 (0.72, 1.16)	1.0 (0.78, 1.28)
Fresh ART	167/528 (31.6%)	3295/10 628 (31.0%)	1.03 (0.79, 1.35)	1.05 (0.79, 1.41)
Frozen ART	45/230 (19.6%)	535/2228 (24.0%)	0.77 (0.47, 1.25)	0.85 (0.51, 1.41)

*Adjustment for confounders (number of previous IVF cycles, previous live birth, year of treatment, day of embryo transfer, number of embryo transferred, fresh and frozen cycle for combined fresh/frozen).
LBR, live birth rate; OR, odds ratio.

Live births after donor oocyte recipient cycle in women with endometriosis versus donor oocyte recipient cycle in women without endometriosis (male factor infertility)

The LBR in women with endometriosis undergoing donor oocyte recipient cycles was lower compared to women undergoing donor oocyte recipient cycles without endometriosis (28.0% vs 30.7%; aOR 0.86, 99.5% CI 0.67 to 1.10) but the difference did not reach statistical significance. The trend toward lower LBR was observed when donor recipient fresh embryo cycles (31.6% vs 34.3%; aOR 0.86, 99.5% CI 0.65 to 1.15) and donor recipient frozen embryo transfer cycles were compared separately (19.6% vs 22.6%; aOR 0.82, 99.5% CI 0.50 to 1.35) (Table IV and Supplementary Table SII).

Table III Live birth rate in women with endometriosis following donor oocyte recipient versus autologous ART cycles (subgroup analysis for period of treatment—1996–2005 and 2006–2016).

	Donor oocyte recipient cycle	Autologous ART cycle	Unadjusted OR (99.5% CI)	Adjusted OR* (99.5% CI)
Year of treatment (1996–2005)				
Fresh and frozen LBR per cycle	49/202 (24.3%)	1105/4071 (27.1%)	0.86 (0.54, 1.38)	1.08 (0.66, 1.79)
Fresh ART	38/145 (26.2%)	977/3437 (28.4%)	0.89 (0.52, 1.54)	1.08 (0.61, 1.92)
Frozen ART	11/57 (19.3%)	128/634 (20.2%)	0.94 (0.35, 2.52)	1.07 (0.38, 2.98)
Year of treatment (2006–2016)				
Fresh and frozen LBR per cycle	163/556 (29.3%)	2725/8785 (31.0%)	0.92 (0.70, 1.21)	0.96 (0.72, 1.28)
Fresh ART	129/383 (33.7%)	2318/7191 (32.2%)	1.07 (0.78, 1.46)	1.03 (0.73, 1.44)
Frozen ART	34/173 (19.7%)	407/1594 (25.5%)	0.71 (0.41, 1.25)	0.78 (0.43, 1.41)

*Adjustment for confounders (number of previous IVF cycles, previous live birth, day of embryo transfer, number of embryo transferred, fresh and frozen cycle for combined fresh/frozen).
LBR, live birth rate; OR, odds ratio.

Table IV Live birth rate in women with endometriosis versus women without endometriosis (male factor) following donor oocyte recipient cycles.

	Oocyte recipient endometriosis	Oocyte recipient without endometriosis	OR (99.5% CI)	Adjusted OR (99.5% CI)*
Fresh and frozen LBR per cycle	212/758 (28.0%)	1816/5917 (30.7%)	0.88 (0.69, 1.12)	0.86 (0.67, 1.10)
Fresh ART	167/528 (31.6%)	1403/4092 (34.3%)	0.89 (0.67, 1.17)	0.86 (0.65, 1.15)
Frozen ART	45/230 (19.6%)	413/1825 (22.6%)	0.83 (0.51, 1.36)	0.82 (0.50, 1.35)

*Adjustment for confounders (number of previous IVF cycles, previous live birth, period of treatment, day of embryo transfer, number of embryo transferred, fresh and frozen cycle for combined fresh/frozen).
LBR, live birth rate; OR, odds ratio.

Discussion

The current study did not find any significant difference in the LBR in women with endometriosis undergoing donor oocyte recipient embryo transfer cycles compared to autologous IVF embryo transfer cycles. Furthermore, no significant difference was observed in the LBR in the subgroup of women with endometriosis undergoing donor oocyte recipient fresh embryo transfer cycles versus fresh autologous IVF fresh embryo transfer cycles. Similarly, the LBR did not differ significantly following donor oocyte recipient frozen embryo transfer cycles versus autologous IVF frozen embryo transfer cycles. Taken together, these findings suggest that there may be a limited or no effect of oocyte quality on IVF outcomes in women with endometriosis.

In a study by Simon *et al.* (1994), the treatment outcomes following oocyte donation according to origin of the oocyte (n = 141) was evaluated. The results of this study reported a significantly lower implantation rate in recipient women who received donated oocytes from women with endometriosis compared to other indications. The authors suggested that poor oocyte quality could have been a reason for the worse treatment outcomes following IVF in women with endometriosis, although the causative role of an endometrial factor was not excluded. However, the number of treatment cycles performed using donor oocyte from women with endometriosis was small (n = 11). Furthermore, other donor oocyte recipient characteristics as well as specific treatment related factors may also have influenced the outcomes. In an interesting matched control study by the same group, 25 women with severe endometriosis (Stages III–IV) and 33 women without endometriosis underwent oocyte donation treatment (Diaz *et al.*, 2000). A single donor donated oocytes to recipient women from both the groups (the sibling oocyte model). The implantation rate (14.8% vs 16%) and LBR (28% vs 27.2%) did not show any significant difference between the two groups. The authors suggested that the likely reason for the poorer outcomes in women with endometriosis is due to suboptimal oocyte/embryo quality and any negative impact on endometrium was not evident in this study. In a matched case controlled study, the authors reported that the donor oocyte IVF treatment outcome was not negatively influenced by the presence of endometriosis in the recipient (Bodri *et al.*, 2007). The findings from these studies are not in agreement with the current study results. The possible reasons could be due to small sample size and differences in the study population. While the study by Diaz *et al.* (2000), included only women with severe endometriosis, the current study analyzed a nationwide dataset in which women with varying severity of endometriosis were included. Increasing severity of endometriosis has been shown to result in a lower LBR following IVF in women with endometriosis (Muteshi *et al.*, 2018).

A recent single-center retrospective cohort study compared treatment outcomes following frozen embryo transfer of euploid blastocysts in women with endometriosis (n = 39) versus two control groups, male factor (n = 253) and preimplantation testing for monogenic disease (PGT-M) (n = 36) (Bishop et al., 2021). The authors found no significant difference in LBR in women with endometriosis (61.1%) compared to male factor (49.6%) and the PGT-M group (52.1%). Since the investigators controlled for embryo quality and reported no significant difference in treatment outcomes in women with endometriosis versus controls, their findings indicated that endometrial receptivity has a limited role in poorer outcomes following IVF in women with endometriosis which is in contrast to the current study finding. While the authors included only surgically confirmed endometriosis, the information relating to the severity of endometriosis was lacking. Furthermore, a smaller sample size and the potential selection bias due to the inclusion of only euploid blastocyst transfers, which are more likely to comprise of women with a better prognosis, could be some of the possible reasons for disagreement with the current study results.

The current study findings suggest impaired endometrial receptivity could be an important reason for poorer IVF outcomes in women with endometriosis. While many non-clinical studies have highlighted the role of aberrant signaling pathways, altered gene expression, chronic inflammation, progesterone resistance and estrogen dominance in making the endometrium less receptive to embryo implantation in women with endometriosis, only a few clinical studies have corroborated these findings (Bulun *et al.*, 2006; Aghajanova *et al.*, 2010; Lessey and Kim, 2017). A large prospective study by Prapas *et al.* (2012) investigated whether endometriosis affects endometrial receptivity using the donor oocyte recipient model. The study population consisted of 240 menopausal women, divided into two groups of those with a history of laparoscopically diagnosed endometriosis and those without. Oocytes derived from a single donor who was diagnosed as free from endometriosis, were randomly divided between the two groups on the day of oocyte retrieval. The LBR was significantly lower in the group of women diagnosed with endometriosis compared to the group without endometriosis (35% vs 50.83%; aOR 0.19, 95% CI 0.09–0.38). The authors attributed these findings to the negative impact of endometriosis on endometrial receptivity itself. However, the current study reported no significant difference in LBR for donor oocyte recipient women with endometriosis compared with the donor oocyte recipient women who do not have endometriosis. This is in disagreement with the study by Prapas *et al.* (2012), and the possible reasons for this could be due to the differences in the study population, use of oocytes from the same donor versus different donor and data from single center versus nationwide dataset. In a retrospective cohort study, Juneau *et al.* (2017) investigated whether oocytes in endometriosis are more susceptible to meiotic error. The authors compared aneuploidy rates in women with endometriosis (n = 305) versus controls (n = 3798) who underwent preimplantation genetic screening cycles. The aneuploidy rates did not differ significantly between both the two groups. The authors suggested that the reason for lower success rate after IVF in women with endometriosis could be multifactorial. The study findings suggest a lesser role of oocyte quality in poor IVF outcomes in endometriosis.

The strengths of the current study include that it is one of the largest studies that has analyzed a nationwide validated dataset, using a donor oocyte recipient versus autologous IVF model. The analysis exclusively included treatment cycles with endometriosis alone as an indication while those cycles with more than one cause of infertility were excluded to avoid confounding variables. To minimize the impact of age-related decline in LBR in the autologous group, we included only women aged <35 years in the autologous IVF cohort whilst in the donor oocyte recipient cohort, the recipients received oocytes from women aged ≤35 years. The results have also been adjusted for other potential known confounders as described in the Results section. We also performed a subgroup analysis to explore possible differences in the results due to the variation in laboratory practices during the two-decade-long study period. Additionally, the inclusion of data from multiple ART centers across the UK increases the generalizability of the current study findings. However, limitations of this study include a lack of data on the method of diagnosis of endometriosis and its severity as well as the presence of coexisting adenomyosis. Furthermore, there was no information as to whether the women donating oocytes were free from endometriosis. There was also a lack of information on oocyte number for the donor recipient cycle, which was an important limitation as it is considered a prognostic factor (Boucret *et al.*, 2020). Limitations of a retrospective design also apply to current study findings. Finally, the anonymized nature of the dataset precluded reporting of cumulative LBR.

In conclusion, the current study findings add further weight to the body of evidence that the reduced LBR seen in women with endometriosis may actually be predominantly due to impaired endometrial receptivity. Whilst we cannot completely rule out the negative impact of oocyte quality on IVF outcomes in women with endometriosis, it may have much smaller role than indicated by earlier studies (Simon *et al.*, 1994; Diaz *et al.*, 2000). Furthermore, this study could not explore the impact of oocyte number on the IVF treatment outcome in women with endometriosis. The current study finding needs to be further validated by similar large dataset studies which have information on the oocyte number and cumulative LBR. The definitive knowledge about the reason for poorer IVF outcomes in endometriosis would help with optimizing treatment outcomes.

Supplementary data

Supplementary data are available at *Human Reproduction Open* online.

Data availability

The anonymized dataset underlying this article is available from HFEA (https://www.hfea.gov.uk/about-us/our-data/).

Acknowledgements

The anonymized dataset was provided by the HFEA.

Authors' roles

M.S.K. conceived the study, directed the analysis and drafted the manuscript. S.K.S. directed the analysis, interpretation and inputted into drafting of the manuscript. V.S. helped in analysis and interpretation,

inputted into the drafting and revision of the manuscript. B.A. performed the analysis and interpretation and drafting. All authors appraised and approved the final manuscript.

Funding

No funding was obtained.

Conflict of interest

M.S.K. is an associate editor with *Human Reproduction Open*. He was not involved in the editorial or peer review process for the manuscript.

References

Aghajanova L, Velarde MC, Giudice LC. Altered gene expression profiling in endometrium: evidence for progesterone resistance. *Semin Reprod Med* 2010;**28**:51–58.

Barnhart K, Dunsmoor-Su R, Coutifaris C. Effect of endometriosis on *in vitro* fertilization. *Fertil Steril* 2002;**77**:1148–1155.

Bishop LA, Gunn J, Jahandideh S, Devine K, Decherney AH, Hill MJ. Endometriosis does not impact live-birth rates in frozen embryo transfers of euploid blastocysts. *Fertil Steril* 2021;**115**:416–422.

Bodri D, Colodron M, Vidal R, Galindo A, Durban M, Coll O. Prognostic factors in oocyte donation: an analysis through egg-sharing recipient pairs showing a discordant outcome. *Fertil Steril* 2007;**88**:1548–1553.

Boucret L, Bouet P-E, Riou J, Legendre G, Delbos L, Hachem HE, Descamps P, Reynier P, May-Panloup P. Endometriosis lowers the cumulative live birth rates in IVF by decreasing the number of embryos but not their quality. *JCM* 2020;**9**:2478.

Bulun SE, Cheng YH, Yin P, Imir G, Utsunomiya H, Attar E, Innes J, Kim JJ. Progesterone resistance in endometriosis: link to failure to metabolize estradiol. *Mol Cell Endocrinol* 2006;**248**:94–103.

den Hartog JE, Lardenoije CM, Severens JL, Land JA, Evers JL, Kessels AG. Screening strategies for tubal factor subfertility. *Hum Reprod* 2008;**23**:1840–1848.

Diaz I, Navarro J, Blasco L, Simón C, Pellicer A, Remohí J. Impact of stage III-IV endometriosis on recipients of sibling oocytes: matched case-control study. *Fertil Steril* 2000;**74**:31–34.

Dunselman GAJ, Vermeulen N, Becker C, Calhaz-Jorge C, D'Hooghe T, De Bie B, Heikinheimo O, Horne AW, Kiesel L, Nap A *et al.* ESHRE guideline: management of women with endometriosis. *Hum Reprod* 2014;**29**:400–412.

Focarelli R, Luddi A, De Leo V, Capaldo A, Stendardi A, Pavone V, Benincasa L, Belmonte G, Petraglia F, Piomboni P. Dysregulation of GdA expression in endometrium of women with endometriosis: implication for endometrial receptivity. *Reprod Sci* 2018;**25**:579–586.

Georgiou EX, Melo P, Baker PE, Sallam HN, Arici A, Garcia-Velasco JA, Abou-Setta AM, Becker C, Granne IE; Cochrane Gynaecology and Fertility Group. Long-term GnRH agonist therapy before *in vitro* fertilisation (IVF) for improving fertility outcomes in women with endometriosis. *Cochrane Database Syst Rev* 2019;**2019**:CD012340.

Harb HM, Gallos ID, Chu J, Harb M, Coomarasamy A. The effect of endometriosis on *in vitro* fertilisation outcome: a systematic review and meta-analysis. *BJOG* 2013;**120**:1308–1320.

Juneau C, Kraus E, Werner M, Franasiak J, Morin S, Patounakis G, Molinaro T, de Ziegler D, Scott RT. Patients with endometriosis have aneuploidy rates equivalent to their age-matched peers in the *in vitro* fertilization population. *Fertil Steril* 2017;**108**:284–288.

Lessey BA, Kim JJ. Endometrial receptivity in the eutopic endometrium of women with endometriosis: it is affected, and let me show you why. *Fertil Steril* 2017;**108**:19–27.

Macer ML, Taylor HS. Endometriosis and infertility: a review of the pathogenesis and treatment of endometriosis-associated infertility. *Obstet Gynecol Clin North Am* 2012;**39**:535–549.

Muteshi CM, Ohuma EO, Child T, Becker CM. The effect of endometriosis on live birth rate and other reproductive outcomes in ART cycles: a cohort study. *Hum Reprod Open* 2018;**2018**:hoy016.

Orazov MR, Radzinsky VY, Ivanov II, Khamoshina MB, Shustova VB. Oocyte quality in women with infertility associated endometriosis. *Gynecol Endocrinol* 2019;**35**:24–26.

Prapas Y, Goudakou M, Matalliotakis I, Kalogeraki A, Matalliotaki C, Panagiotidis Y, Ravanos K, Prapas N. History of endometriosis may adversely affect the outcome in menopausal recipients of sibling oocytes. *Reprod Biomed Online* 2012;**25**:543–548.

Senapati S, Sammel MD, Morse C, Barnhart KT. Impact of endometriosis on *in vitro* fertilization outcomes: an evaluation of the Society for Assisted Reproductive Technologies Database. *Fertil Steril* 2016;**106**:164–171.

Simon C, Gutiérrez A, Vidal A, de los Santos MJ, Tarín JJ, Remohí J, Pellicer A. Outcome of patients with endometriosis in assisted reproduction: results from *in-vitro* fertilization and oocyte donation. *Hum Reprod* 1994;**9**:725–729.

Sunkara SK, Antonisamy B, Redla AC, Kamath MS. Female causes of infertility are associated with higher risk of preterm birth and low birth weight: analysis of 117 401 singleton live births following IVF. *Hum Reprod* 2021;**36**:676–682.

Wei Q, St Clair JB, Fu T, Stratton P, Nieman LK. Reduced expression of biomarkers associated with the implantation window in women with endometriosis. *Fertil Steril* 2009;**91**:1686–1691.