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Correlation of IVF outcomes and number of oocytes retrieved: a UK retrospective longitudinal observational study of 172 341 non-donor cycles

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ABSTRACT

Objective How do numbers of oocytes retrieved per In vitro fertilisation (IVF) cycle impact on the live birth rate (LBR) and multiple gestation pregnancy (MGP) rates?

Design Retrospective observational longitudinal study.

Setting UK IVF clinics.

Population Non-donor IVF patients.

Main outcome measures LBR per IVF cycle and MGP levels against number of oocytes retrieved into subgroups: 0, 1–5, 6–15, 16–25, 26–49 oocytes and 50+ oocytes. Relative risk (RR) and 95% CIs were calculated for each group against the intermediate responder with '6–15 oocytes collected'.

Results From 172 341 attempted fresh oocyte retrieval cycles, the oocyte retrieved was: 0 in 10 148 (5.9%) cycles from 9439 patients; 1–5 oocytes in 42 574 cycles (24.7%); 6–15 oocytes in 91 797 cycles (53.3%); 16–25 oocytes in 23 794 cycles (13.8%); 26–49 oocytes in 3970 cycles (2.3%); ≥50 oocytes in 58 cycles (0.033%). The LBRs for the 1–5, 6–15, 16–25 and 26–49 subgroups of oocytes retrieved were 17.2%, 32.4%, 35.3% and 18.7%, respectively. The RR (95% CI) of live birth in comparison to the intermediate group (6–15) for 1–5, 16–25 and 26–49 groups was 0.53 (0.52 to 0.54), 1.09 (1.07 to 1.11) and 0.58 (0.54 to 0.62), respectively. The corresponding MGP rates and RR were 9.2%, 11.0%, 11.4% and 11.3%, respectively and 0.83 (0.77 to 0.90), 1.04 (0.97 to 1.11) and 1.03 (0.84 to 1.26), respectively.

Conclusion There was only limited benefit in LBR beyond the 6–15 oocyte group going to the 16–25 oocytes group, after which there was significant decline in LBR. The MGP risk was lower in 1–5 group.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ Largest aggregate UK statutory national data analyses on oocyte numbers retrieved ensures a high degree of applicability.
⇒ Unique insight into UK real-time in vitro fertilisation (IVF) ovulation induction practices revealing the numbers of oocytes being retrieved along their associated subgroups live birth rate and risks of multiple gestation pregnancy.
⇒ Biases in data collection is minimal as data are gained independently under the UK Freedom of Information Act 2000 from the statutory Human Fertilisation & Embryology Authority body.
⇒ Retrospective and observational study.
⇒ Potential confounders associations such as age, other demographics, clinical conditions and procedures unavailable.

INTRODUCTION

Live birth rates (LBRs) have been calculated according to the number of oocytes retrieved per cycle and this process has been the subject of a continuous debate over the last decade.[1–6] Data on the associated risks of ovarian hyperstimulation syndrome (OHSS) and the perinatal complications of multiple gestation pregnancy (MGP) are limited following oocyte retrieval, particularly for oocyte harvesting after extremely intense hyperstimulation.[7–13] This is mainly due to most authors focusing on the technical aspects of IVF such as frozen embryo transfer cycles (FER) which are assumed to be single embryo transfer (SET) cycles only. Whereas LBRs appear to be the primary driving factor to persuade patients to select a particular clinic, the risks of OHSS and MGP, but also the added costs and cost effectiveness to achieve an optimal LBR are rarely included in the debate. Overall, this limits access to accurate data for couples undergoing artificial reproductive treatments (ARTs) to make informed choices.

Women undertaking controlled ovarian stimulation are broadly categorised as poor, normal and high responders. The age of the patient and her ovarian reserve may contribute to determine the category and high responders tend to be generally younger and present with higher ovarian reserve.[14 15] The number of oocytes needed to achieve

optimal LBR remains difficult to evaluate. Most studies indicate that an optimal LBR can be obtained during fresh cycles with 8–18 oocytes retrieved.[5 7 13 16] A study of 65 868 singleton births after fresh embryo transfer (ET) has shown that an excessive ovarian response, that is, when >20 oocytes are retrieved for IVF, is associated with an increased risk of preterm birth (PTB) and low-birth weight (LBW).[8] By contrast, a more recent study including 27 359 singleton babies born after fresh IVF cycles found no association between the number of oocytes retrieved and neonatal outcomes, including PTB, small-for-gestational age, perinatal/neonatal death, major birth defects and the number of oocytes retrieved.[17]

The main objective of our study was to evaluate the relationship between the number of oocytes retrieved in non-donor IVF cycles and LBR and risks such as MGP rates in a large population database.

METHODS AND MATERIALS

Study population

This is a retrospective longitudinal observational cohort study. Anonymised data were obtained through the Freedom of Information Act (FOI, 2000) from the Human Fertilization and Embryology Authority (HFEA) live database in February 2021 for all IVF and intracytoplasmic sperm injection (ICSI) non-donor and non-oncology IVF cycles performed in the UK during a 4-year period from 2015 to 2018. The HFEA is an executive non-departmental public body of the Department of Health and Social Care and the statutory regulator of assisted reproductive technology (ART-IVF, ICSI and intrauterine insemination (IUI)) treatment in the UK (www.hfea.gov.uk HFEA authority). Submission of data to the HFEA is mandatory for all UK clinics and failure to report results can lead to the revocation of the clinic licence for serious breaches. The HFEA collects information on all ART treatment cycles performed by 86 licensed public and private fertility clinics across the UK. Data were collected independently by HFEA staff, unaware of the objective of our study thereby removing bias. The HFEA provided a summary of the data in tabulated form which restricted interrogation of data. Data on OHSS were requested but were unavailable from the HFEA.

Information was obtained on the number of fresh oocytes retrieved and embryos obtained, transferred and stored during the treatment period 2015–2018 either in fresh or frozen cycles. The data on ART cycles provided were stratified according to the number of oocytes retrieved per cycle into the following subgroups: none, 1–5 oocytes (low responder), 6–15 oocytes (intermediate responder), 16–25 oocytes (high responder), 26–49 oocytes (very high responder) and >50 oocytes (extremely high responder). Only IVF/ICSI studies with homologous gametes were analysed. The dataset included the total number of oocytes collected and numbers of embryos created from 2015 to 2018 and the live database analysed in February 2021 thereby providing a reasonable estimate of the biological efficiency from oocyte to embryos to a live birth.

Randomisation and masking

The very large data gained under the FOI 2000 and derived independently by HFEA personnel do not have the requirements for randomisation or masking as for randomised control trials (RCTs) where small numbers are considered.

Limitation of the UK FOI dataset is associated with the limits of clinical data and patient details available and a repeat request will lead to small variation due to the nature of the live database. The data do not interrogate clinical background of patients or the segregation of IVF and ICSI data. The patient demographic data were limited, and no data could be obtained on OHSS rates, diagnosis or stimulation methods, stillbirths, use of ICSI, eSET cycles and fresh or frozen IVF cycles, number of oocytes and embryos frozen, and use of add-on and selection procedures. For MGP levels, the number of embryos transferred is unavailable and whether fresh or frozen embryos were used.

Procedures

The procedures are fully described under Methods section.

The procedure of data collection was through FOI requests from the UK HFEA collecting information as part of its regulatory remit and for the purpose of issuing a licence to clinics to operate. There is therefore no scope for clinics to selectively submit or withhold their activities or outcome data.

The HFEA provided a summary of the data in tabulated form which also restricts further interrogation of data or the way statistics can be performed.

None of the authors could influence the dataset or the way data could further inclusion/exclusion choices, as this was handed over under FOI by the HFEA. No UK clinic could selectively submit data to the HFEA. Submission is a statutory obligation, resulting in revocation of the clinic licence for serious breaches.

Outcomes

The primary outcome was LB per cycle and MGP levels according to the subgroups having 1–5 oocytes (low responder), 6–15 oocytes (intermediate responder), 16–25 oocytes (high responder), 26–49 oocytes (very high responder). The period of study was 2015–2018, the live database analyses of LBR and MGP were performed where ET had occurred by February 2021.

Subgroups with 0 and 50+ oocytes were excluded from the analysis except for the description of oocyte group distribution.

Statistical analysis

Relative risk (RR) and 95% CIs were calculated for each subgroup in comparison with the data of the intermediate responder (6–15 oocytes retrieval) subgroup which was used as a reference. The main outcome measures was

Table 1 Number of cycles for each group, stratified according to the number of oocytes retrieved

Number of oocytes collected	Total cycles	% cycles
0	10148	5.9
1–5	42574	24.7
6–15	91797	53.3
16–25	23794	13.8
26–49	3970	2.3
50–59	38	0.02
60+	20	0.01
	172341	

Distribution of number of cycles correlated to number of oocytes retrieved.

the LBR per treatment cycle. The secondary outcome measure was MGP per live births. A p value of <0.05 was considered statistically significant.

The data on IVF cycles provided were stratified according to the number of oocytes retrieved per cycle into the following subgroups: none, 1–5 oocytes (low responder), 6–15 oocytes (intermediate responder), 16–25 oocytes (high responder), 26–49 oocytes (very high responder) and >50 oocytes (extremely high responder). Only IVF/ICSI studies with homologous gametes were analysed. Analyses were conducted using SPSS V.26 (IBM Corp., USA).

Patient and public involvement

No patient involved.

RESULTS

There were 172341 fresh oocyte retrieval cycles during the study period including: none in 10148 (5.9%) cycles in 9439 patients; 1–5 in 42574 cycles (24.7%); 6–15 in 91797 cycles (53.3%); 16–25 in 23794 cycles (13.8%); 26–49 in 3970 cycles (2.3%); ≥50 in 58 cycles (0.033%) (table 1, figure 1). After 3–6 years follow-up, the biological conversion efficiency from oocytes collected per cycle and embryos conceived by IVF resulting in an LB was 2.8% and 4.9%, respectively. The raw data obtained from the HFEA are presented in table 2.

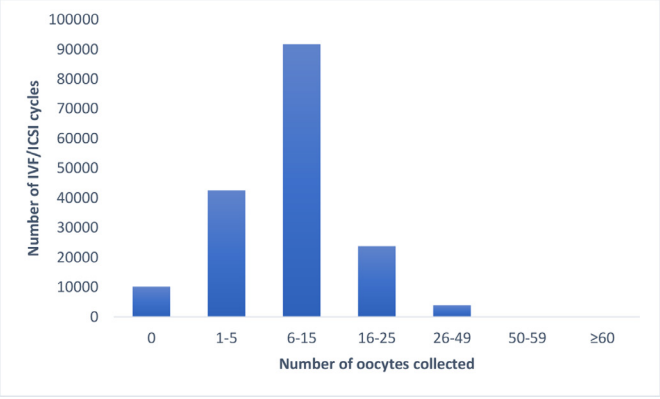

Figure 1 Number of IVF cycles per each category of number of retrieved oocytes. Graphical distribution of number of cycles correlated to number of oocytes retrieved. IVF, in vitro fertilisation; ICSI, intracytoplasmic sperm injection.

The success rate of LBR per cycle is shown in table 2 and the statistical relationships between LBR and MGP rate and the number of oocytes retrieved per cycle are shown in table 3. The LBRs for the subgroups were 17.2%, 32.4%, 35.3% and 18.7%, respectively (figure 2). The LBR per cycle increased significantly (p<0.05) from 1–5 and 6–15 to 16–25 but declined significantly (p<0.05) for the 26–49 oocyte subgroup. Compared with the reference subgroup, the RRs for the 1–5, 16–25 and 26–49 oocytes subgroups were 0.53 (0.52 to 0.54), 1.09 (1.07 to 1.11) and 0.58 (0.54 to 0.62), respectively.

In the study period, 5.9% failed oocyte retrieval cycles were associated with 9439 women and of which cohort 7.5% of the women endured repeated failed cycle (tables 1 and 2).

Table 3 displays the MGP rates. MGP rates for 1–5, 6–15, 16–25, 26–49 oocytes subgroup and RRs were 9.2%, 10.9%, 11.4% and 11.3%, respectively. The MGP rates increased significantly (p<0.05) from the 1–5 to the 6–15 oocytes subgroup and subgroups above. Thus the MGP data, however, are not significant between the last two groups 16–25 and 26–49 oocyte subgroups. Compared with the reference subgroup, the RRs for the 1–5, 16–25 and 26–49 oocytes subgroups were 0.83 (0.77 to 0.90), 1.04 (0.97 to 1.11) and 1.03 (0.84 to 1.26), respectively.

The biological efficiency from 1624912 oocytes retrieved led to 931265 embryos (57.31% conversion rate). The LB occurrence from oocytes collected was 2.84%, whereas from embryos created was 4.96%.

DISCUSSION

Our analyses of the live HFEA dataset on non-donor IVF cycles performed 3–6 years post oocyte retrieval for the period between 2015 and 2018 shows the distribution of oocytes retrieved (table 1, figure 1). The data indicate that the LBR varies according to the number of oocytes retrieved per cycle and that the highest success rate (35.3%) is found when 16–25 oocytes retrieved. Although the LBR was higher (32.4%) for the group of 6–15 oocytes, the success rate was lower for the low-responders and high-responders when the number of oocytes retrieved was ≤5 oocytes (17.22%) and ≥26 oocytes (18.71%), respectively (table 2). The association between the number of oocytes retrieved per cycle and subsequent LBR is well established, however, as far as we know, our study is the first to show a significantly (p<0.05) lower success rate for the extremely high responders. By contrast, we found that the rate of MGP remained similar between the low responders (9.15%), the normal responders (11.41%) and high responders (11.31%) (tables 2 and 3). The high levels of MGP suggest that eSET practices are less

Table 2 HFEA outcome data obtained for the study period

							Total/comment
Number of oocytes collected	0	1–5	6–15	16–25	26–49	>50	
Total cycles*	10 148	42 574	91 797	23 794	3970	58	162 135
Total number of oocytes	N/A	N/A	N/A	N/A	N/A	N/A	1 624 912
Total number of embryos created		N/A	N/A	N/A	N/A	N/A	931 265
% Conversion to embryos from oocytes		N/A	N/A	N/A	N/A	N/A	57.31%
Embryos frozen for own use	N/A	N/A	N/A	N/A	N/A	N/A	219 563
% Embryos created frozen	N/A	N/A	N/A	N/A	N/A	N/A	23.58%
Total patients*	9439	38 027	83 983	23 172	3929	58	149 111
Live birth occurrence	N/A	7330	29 729	8395	743	N/A	46 197
% LB occurrence from embryos created		N/A	N/A	N/A	N/A	N/A	4.96%
LBR/cycle	N/A	17.22	32.39	35.28	18.71	N/A	
MGP	N/A	671	3262	958	84	N/A	4975
MGP rate	N/A	9.15	10.97	11.41	11.31	N/A	
Patients with repeat cycles	709	N/A	N/A	N/A	N/A	N/A	
Number of oocytes equivalent for 1 LB		N/A	N/A	N/A	N/A	N/A	35.2
LB from oocytes collected	N/A	N/A	N/A	N/A	N/A	N/A	2.84%
Biological wastage from oocyte retrieval (real-time status)		N/A	N/A	N/A	N/A	N/A	97.16%

Data provided by the HFEA under the FOI Act 2000.
*Final total excludes 0 oocytes and 50+ oocytes cycles in final total value.
HFEA, Human Fertilisation & Embryology Authority; LBR, live birth rate; MGP, multiple gestation pregnancy; N/A, not available.

likely practised with the available quality of embryos from the higher responder groups. Over 2.3% of IVF cycles performed led to 26 to >60 oocytes retrieved (table 1, figure 1). Failure to retrieve oocytes adversely affected 9439 women, who underwent 10 148 failed cycles, with 709 women (7.5% of cohort) having undergone repeated failed cycles (table 2). Failure to retrieve cycles needs more critical analyses and openness given the reliance on ovarian reserve markers, the costs and trauma patients endure.

How many is too many?

The finding of highest LBR in high responder group of 16–25 eggs collected can be explained by the fact that there would be more embryos for cryopreservation for subsequent FER than for the low and normal responders. A previous large study[1] using the HFEA data from the 1991–2008 period has shown that the LBR increases with number of oocytes up to 15, plateauing between ~15 and 20 oocytes, and steadily decline beyond 20 oocytes.[1] However, the authors could not evaluate the LBR rates based on data available at the time. The low LBR in the extremely high responders could be due to poor egg and embryo quality but more probably are associated with high oestradiol concentration secondary to over stimulation.[18 19] Furthermore, high ovarian response is often complicated by Polycystic ovary syndrome (PCOS) and can lead to a higher likelihood of freeze-all cycles.[20] The proportion of euploid embryos per oocyte yield or stimulation dose remains small.[21–23] The larger the number of retrieved oocytes, the higher the number of immature oocytes and the number of oocytes failing to produce an embryo.[24] These findings suggest that stimulation protocols appear to rely on data from retrospective studies prompting the 'more is better' approach needs changing.

We found a higher LBR in high responders, however, this should not lead to the use of a stimulation regimen

Table 3 Statistical relationship between different oocyte retrieval groups

	RR (95% CI) (1–5 vs 6–15)	RR (95% CI) (16–25 vs 6–15)	RR (95% CI) (26–49 vs 6–15)
LBR/cycle	0.53 (0.52 to 0.54); p<0.0001	1.09 (1.07 to 1.11); p<0.0001	0.58 (0.54 to 0.62); p<0.0001
MGP rate	0.83 (0.77 to 0.90); p<0.0001	1.04 (0.97 to 1.11); p=0.26	1.03 (0.84 to 1.26); p=0.77

Comparison of main outcome measures depending on the number of oocytes retrieved. The statistical relationships between LBR and MGP and oocytes retrieved.
LBR, live birth rate; MGP, multiple gestation pregnancy; RR, relative risk.

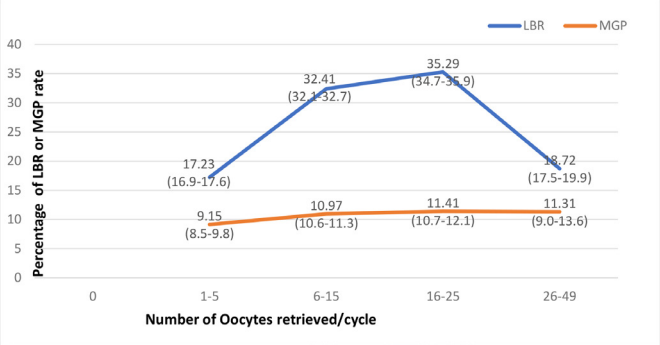

Figure 2 LBR and MGP rates (with 95% CI) per cycle against oocyte numbers retrieved. Correlation of oocyte numbers retrieved groups against LBR and MGP rates. LBR, live birth rate; MGP, multiple gestation pregnancy.

that increases oocyte numbers beyond the 15-oocyte mark as it is associated with an increased risk of OHSS. In addition, our data indicate that beyond the 15-oocyte collection mark there is a significant increase in MGP rates, while the LBR declines significantly beyond 25-oocytes (table 3). The biological conversion efficiency from oocytes to achieving an LB potentially drops as the number of retrieved oocytes increases as shown from lower LBR in the very high responders (figure 2). Previous studies have not reported on the MGP rates against oocyte numbers retrieved. In the present study, we show that MGP rates remain similar, but nationally high, in the normal, high and extreme high responders. Despite the widely adopted elective SET (eSET) protocol in women of ≤35 years in the UK, the high MGP rates in the HFEA database suggest that eSET is not widely practised. By contrast, the higher rates of MGP after higher oocytes collected subgroup suggest that the oocyte and subsequent embryo qualities are poor which may explain why many IVF clinics perform multiple ET with MGP rates well above those resulting from spontaneous conception. MGP rates in subgroups where >15 oocyte was collected per cycle oppose the concept that collecting more oocytes will lead to greater embryo choices which improve success rates. The likelihood of double or triple ET for low responder group due to embryo quality and quantity is well known and is associated with the lowest LBR. Our findings suggest that there is a rate limiting factor above which either oocyte competency or embryo qualities are compromised.

Biological and clinical efficiencies

Overall, our data indicate that the level of biological inefficiency of converting oocytes and embryos into an LB is 2.8%. This shows that failure rate is 97.2% from oocytes collected and <5% of all embryos resulting from IVF result in an LB. These data suggest that there is an oocyte competence factor which may compromise embryo quality, and thus LBR. The conversion from oocytes to LB has previously been set at 5%[25] whereas in a donor model, the oocyte-to-LBR was found to be 6.5%.[26] Compared with pioneering days of IVF, there is evidence that the efficiency of oocyte utilisation rates has declined[27] despite the use of numerous non-evidence-based add-on procedures and tests. Unlike previous studies, our contemporary data analysis coincides with a period with add-on practices being used to optimise LBRs and minimise MGP, but these add-ons appear to benefit minimally.

Most patients would likely have undergone ET as there is a 3–6-year post oocyte retrieval time lapse. Previous studies have challenged the concept that the higher the number of oocytes collected per cycle the higher the LBR. Of 7422 women undergoing oocyte retrieval, only 24% conceived with the highest pregnancy rates observed when 13 oocytes were retrieved.[16] A previous analysis of the HFEA data from 1991 to 2008 found that an average of 15 oocytes per cycle was optimal for the LBR.[1] This large timespan of 1991–2008 was gained from a static database with self-selected cases. Furthermore, IVF practices have changed so much and where MGP and OHSS levels would have been higher than in the 2015–2018 period of our study. Furthermore, the definitions of, for example, infertility and male factor have been in a state of flux, while reporting to the HFEA over the 1991–2008 has at best been variable. By contrast, our study reflects contemporary practices, and our dataset was retrieved from a live database by independent HFEA personnel. In a separate analysis of 14 469 patients from 2009 to 2014, 20 oocytes retrieved appeared optimal for a cumulative LBR, declining thereafter, although >25 oocytes were considered to increase cumulative LBR for 'freeze-all' cycles.[6] A >16 oocytes retrieved appeared optimal although the study had sparse data beyond 15 oocytes.[28] There is some evidence that women with ≥11 oocytes retrieved have compromised cytoplasmic immaturity explaining lowered fertilisation and implantation rates.[29] In a mild stimulation protocol on 862 cycles, a 12-oocyte number was found to be optimal for an LB.[24] These findings suggest that the widely held concept that having more embryos to choose from needs to be re-evaluated as embryo morphology alone is limited in predicting a successful LB. Although the vast numbers of oocytes and embryos created, it is clear that the biological efficiency to achieving a live birth remains poor at only 4.96% from embryos created, and of 2.84% from oocytes collected (table 2). The dataset does not reveal the level of the freezing oocytes and embryos and its use, but most frozen material is widely expected to be discarded in the long term. For this reason, patients need to be counselled accordingly and to have a realistic expectation of using frozen material especially after 3–6 years of oocyte retrieval and especially for fertility patients not receiving damaging treatments such as with cancers.

Although we found that 16–25 oocytes per retrieval cycle is optimal for an LBR, this was associated with significant increase in the rate of MGP. Neonatal risks in singleton births where excessive ovarian response, that is, when >20 oocytes have profound increased risk of PTB and LBW,[8] although unproblematic in another report.[17] Our data also inform that there was a significant decline in LBR beyond the 16–25 oocyte retrieval mark suggesting there

may be compromising the oocyte at levels unknown yet. We previously found that in 2016 the MGP rate was 10.9% with a direct cost burden for MGP resulting from IVF of £115 million in the UK.[14] Milder stimulation protocols and reduced gonadotrophins will likely benefit patients outcomes and also financially. Furthermore, there has been an increase in the numbers of IVF cycles performed as a primary treatment and there is a likelihood that many potentially good responders to IUI are offered IVF as a primary therapeutic approach.[14] High oocyte yield is often found in patients with adequate ovarian reserve. Thus, when the male partner presents with adequate semen analysis, milder stimulation protocols or less risky and cost effective IUI cycles should be the primary therapeutic approach.[14 24]

Future practice and policy outlook

The HFEA did not provide data on OHSS or outcomes for the >50 oocyte subgroup for our study. This was because small numbers could potentially breach confidentiality. It is possible that in the last decade, the switch over to antagonists' use has reduced the OHSS risks. However, a recent report has shown that severe OHSS and MGP levels remains high despite eSET practices being preferred.[14] Cycles with significantly high ovarian response are associated various health risks for both patients and offspring other than OHSS but these data are also lacking. High numbers of oocytes retrieved have impact on embryology laboratory time, staffing needs, cost of additional culture dishes, media used, freezing procedures and maintenance. Furthermore, the added cost associated with FET cycles have never been included in cost effectiveness studies. The cost of freezing excess oocytes and embryos is often absent from cost evaluation as is the added technical costs of FER cycles. The impact of intense egg collections on ovarian biology and future egg quality due to excessive oxidative stress damage to the ovary blood supply and on the health of the patient including pain and bruising, are rarely taken into consideration in most studies. Any benefit of choosing from a greater pool of embryos of having more euploid embryos is negatively balanced by the higher rate of MGP and declining LBR with higher oocyte numbers. In addition, the couple counselling suggesting that the 'more oocytes is better' is misleading and psychologically harmful and unethical in generating false hope to achieve a successful pregnancy. Another important consideration relates to extreme >50 oocyte retrieval and the absence of short-term and long-term follow-up information on the health and welfare of these women.

Strengths and limitations

To the best of our knowledge, this study is the largest non-donor aggregate number of IVF treatment cycles showing the association between the number of oocytes retrieved and the LBR and MGP rates, thus reflecting the efficiency of IVF practices. The contemporary period of 2015–2018 also means IVF practices and subfertility definitions are more uniform compared with other studies. The data size provides a reliable baseline information and generalisability on the extent of oocyte retrieval practices and the biological limitations in delivering an LB and enable the evaluation of current clinical management practice. The dataset also provides for baseline failure to retrieve oocytes. The dataset was independently obtained directly from the UK regulatory body thus overcoming selection biases at several levels and ensuring a high degree of applicability of the study results. The 3–6 years post oocyte retrieval follow-up gives a reasonable timeline for fresh or frozen ET to have occurred. While desirable to have a prospective RCT, the size of the dataset is unlikely to match this aggregate dataset analysis.

The main limitations of our study are its retrospective design and the unavailability of associated clinical data such or the segregation of IVF and ICSI data. The patient demographic data were limited, and no data could be obtained on OHSS rates, diagnosis or stimulation methods, use of ICSI, eSET cycles and fresh or frozen IVF cycles, number of oocytes and embryos frozen, numbers and quality of embryos transferred, repeat cycles and use of add-on and selection procedures. The HFEA FOI data are not continuous and therefore limited to calculating adjusted RR using a regression analysis. However, the calculated RR as χ^2 test showed a significant association between the number of oocytes retrieved and LBR and MGP rates, and this gives a more valid comparison between the groups stratified according to the number of oocytes retrieved.

In summary, the study highlights two risk factors: that an embryo derived from a high oocyte retrieval cohort may not be as beneficial as previously thought, and second, the likelihood of compensating any erosion of embryo quality from high oocyte cohort may tempt practitioners to transfer more embryos thereby heightening the risk of MGP. Clearly, there is a need to review UK ovarian stimulation practices and to adopt milder protocols in most cases given the high level of biological inefficiencies in achieving an LB. Current practices suggest an equivalence of 35 oocytes to achieve one LB and this surely can be improved. Within limits of this study there is a need for practice and policy review to reduce the numbers of oocytes being retrieved in IVF treatments and one which is likely to reduce the maternal and neonatal risks.

CONCLUSION

For UK IVF practices, there appears minimal benefit in LBR successes when going from the 6–15 oocyte group to the 16–25 oocyte cohort considering the significantly increased mitigating risk of MGP, and a significant LBR decline for the 26–49 oocytes subgroup. Beyond 6–15 oocytes, subgroups with >15 oocytes retrieved were associated with significantly higher MGP rates, and which for normal and high responder was 11.31%–11.41% compared with the low responders' group at 9.15%. There was significant decline in LBR for the 26–49 and

the ≤5 oocytes subgroups. The biological wastage from oocytes and embryos to eventual LB was extremely high; 2.84% from oocytes collected and 4.96% from all embryos.

The stimulation patterns across the UK in 2015–2018 provided a baseline failure to retrieve oocytes at 5.9% of all cycles, while on the other extreme showing disproportionate practices which led to high and very high responders. Overall, 69% of patients failed to have a baby through IVF procedure and collectively these need to be factored in future cost effectiveness studies and couple counselling, including alternative fertility treatment options prior to starting an IVF treatment.

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