Original Article

Cumulative live-birth rate per ovum pickup in patients with different causes of infertility undergoing in vitro fertilization and embryo transfer: A retrospective study

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Abstract

Aims: To evaluate whether the various causes of infertility have an impact on cumulative clinical pregnancy rate (CCPR) and cumulative live-birth rate (CLBR) following first ovum pickup. **Settings and Design:** A retrospective cohort study between January, 2015 and December, 2018 at the tertiary assisted reproductive technology (ART) Centre in northern India (Jindal IVF and Sant Memorial Hospital, Chandigarh). **Materials and Methods:** A total of 788 patients who underwent first oocyte retrieval during the study period were included based on selection criteria. All patients were divided into various diagnostic categories. All ovum pickup along with subsequent fresh- and frozen-embryo transfer attempts (maximum three) till: a) attained a clinical pregnancy; b) attained a live birth; or c) all the embryos were transferred. The data were analyzed using SPSS-22. The descriptive and comparative analysis was performed using one-way analysis of variance. **Results:** The overall CCPR and CLBR were 54.82% and 50.63%, respectively. The live-birth rates were lowest in patients with the diagnosis of poor responders (25%) and those with genital tuberculosis (37.78%) and highest in those patients with endometriosis (64.10%) and male factor infertility (64.71%).

Keywords: Cumulative clinical pregnancy rate, cumulative live-birth rate, diagnostic categories

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INTRODUCTION

The concept of cumulative live-birth rate (CLBR) is very appealing, but defining CLBR can be a major challenge. Currently, there is no consensus on the most appropriate numerator and denominator for the CLBR. The numerator could be the first live delivery with at least one live-born baby[1,2] or all live deliveries[3] per woman undergoing assisted reproductive technology (ART) treatment. The denominator could be women who initially sought treatment, women who have undergone ovarian stimulation, or all of those who have undergone oocyte retrieval.[4]

For both clinicians and patients, an ideal outcome is the one which provides a meaningful summary of the effectiveness of the treatment. From the patients' perspective, the

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CLBR is more important as it better summarizes the chance of a live birth over an entire treatment period.[5,6] For clinicians, CLBR per oocyte retrieval is more meaningful as it is a much better indicator of quality and success in *in vitro* fertilization (IVF) in its totality as the cryopreservation has become a part of IVF.[7,8]

This retrospective study is aimed at providing more comprehensive information in counseling the patient about the potential for success or prognosis depending upon the etiology of infertility. This is achieved by evaluating the outcome of subsequent embryo transfer attempts from single ovum pickup, that is, the cumulative clinical pregnancy rate (CCPR) and the CLBR per ovum pickup. This may prove to be the most relevant standard of success and can be regarded as a benchmark for any ART center.

SUBJECTS AND METHODS

A retrospective cohort study including patients who underwent first oocyte retrieval between January, 2015 and December, 2018 at a tertiary ART center in northern India (Jindal IVF and Sant Memorial Hospital, Chandigarh). The inclusion criteria were as follows: All ovum pickup (OPU) along with subsequent fresh- and frozen-embryo transfer attempts (maximum 3) till:

(a) attained a clinical pregnancy;
(b) attained a live birth; or
(c) all the embryos were transferred.

The exclusion criteria were as follows:

(a) no embryo transfer performed after OPU;
(b) women who underwent one or more embryo transfers (maximum three) after the index OPU with no successful results but all embryos were not transferred;
(c) donor gametes (sperm or oocyte); and
(d) no embryos available after OPU for transfer (fertilization failure).

All patients undergoing IVF were divided according to various diagnostic categories as follows:

(a) isolated polycystic ovarian syndrome: as defined by NIH 2012;
(b) endometriosis without tubal involvement;
(c) poor ovarian reserve;
(d) tubal factor alone;
(e) genital tuberculosis;
(f) male factor;
(g) unexplained; and
(h) Multifactorial: both male and female factors present or more than one factor in female partner [e.g., polycystic ovarian syndrome (PCOS)+male factor − multifactorial; but there will be no repetition of cases].

Data collection

The data were collected from the hospital ART records and information regarding the age of the patient, cause of infertility, previous pregnancy (primary vs. secondary infertility), number of embryo transfer attempts, and outcomes of pregnancy (biochemical, ectopic, miscarriage, or live birth.

The main outcomes measured were:

(a) CCPR per OPU: It is defined as visualization of gestational sac with fetal heart beat by transvaginal ultrasound (TVS) per number of women who underwent OPU.
(b) CLBR per OPU: It defined as number of live birth per number of women who underwent OPU.

Statistical analysis

The data were analyzed using SPSS-22 [International Business Machines (IBM), Statistical Package for the Social Sciences (SPSS) Statistics]. The descriptive and comparative analysis was performed using one-way analysis of variance.

RESULTS

A total of 959 women underwent oocyte retrieval during the study period (after excluding donor gametes). About 171 patients were excluded from analysis as follows:

(1) In 28 patients, no embryos were available for transfer due to fertilization failure.
(2) In four patients, no embryo transfer was carried out till date.
(3) About 139 patients were excluded in whom all frozen embryos were not used.

Hence, a total of 788 women were included in the further analysis.

The participating individuals were classified based on different etiologies of infertility. The CCPR and CLBR after one complete ART cycle including fresh- and/or subsequent frozen-thaw cycles from first oocyte retrieval per allocated woman according to different causes of infertility are summarized in Table 1.

All diagnoses were cumulatively compared to other diagnosis. It was found that there is a significant difference ($P < 0.05$) in the clinical pregnancy rate of patients with poor ovarian reserve when compared

with PCOS, male factor, and unexplained infertility. Significant difference in CPR was also found when patients with tuberculosis were compared with male factor infertility.

When comparisons were made between different etiologies according to the CLBR, a significant difference was found when endometriosis was compared with poor ovarian reserve; and when the results of LBR in tuberculosis was compared with male factor infertility, that is, *P*-value < 0.05.

The live-birth rates were lowest in patients with the diagnosis of poor responders (25%) and those with genital tuberculosis (37.78%). The overall CCPR and CLBR in our study was 54.82% and 50.63%, respectively. The CPR and LBR after one embryo transfer was 33.63% and 32.36%, respectively, which increased to 50.38% and 47.46% after two embryo transfers and further increased to 54.82% and 50.63% after three embryo transfers. However, clinical pregnancy rate per embryo transfer is 35.94% and live-birth rate per embryo transfer is 33.19% [Figure 1].

DISCUSSION

Most of the studies in the literature have reported pregnancy rates and live-birth rates per treatment cycles. Witsenburg *et al.*[9] reported a CLBR of 59.1% per patient which was reached after seven cycles. A Swedish study reported the CLBR of 55.5% after three completed cycles.[10] In 1999, Engmann *et al.* described a CLBR of 48.2% after three cycles of treatment.[11] Elizur *et al.*[12] reported a cumulative delivery rate of 87% after up to 14 cycles. The study by Malizia *et al.*[5] described CLBRs in IVF in around 6000 patients and showed CLBRs of 51% and 72% with the conservative and optimistic analysis, respectively, after six cycles.

However, reporting on the basis of CCPR and CLBR per complete treatment cycle (i.e., live birth resulting from all fresh- and/or frozen-thawed embryo transfer cycles after one oocyte retrieval) will reflect the efficiency of ART treatment and can be an optimal measure for advising couples seeking infertility treatment. Thus, CLBRs are increasingly replacing the per-cycle-based estimates.

Table 1: Cumulative outcome diagnostic category wise

Diagnostic category	*N*	CCPR		CLBR	
		Mean	SD	Mean	SD
Tubal	80	55.00%	50.06%	50.00%	50.32%
Endometriosis	39	66.67%	47.76%	64.10%	48.60%
Poor ovarian reserve	48	29.17%	45.93%	25.00%	43.76%
PCOS	120	58.33%	49.51%	55.83%	49.87%
Tuberculosis	45	37.78%	49.03%	35.56%	48.41%
Male factor	85	69.41%	46.35%	64.71%	48.07%
Multifactorial	310	53.23%	49.98%	49.03%	50.07%
Unexplained	61	60.66%	49.26%	52.46%	50.35%
Total	788	54.82%	49.80%	50.63%	50.03%

CCPR, cumulative clinical pregnancy rate; CLBR, cumulative live-birth rate; PCOS, polycystic ovarian syndrome; SD, standard deviation.

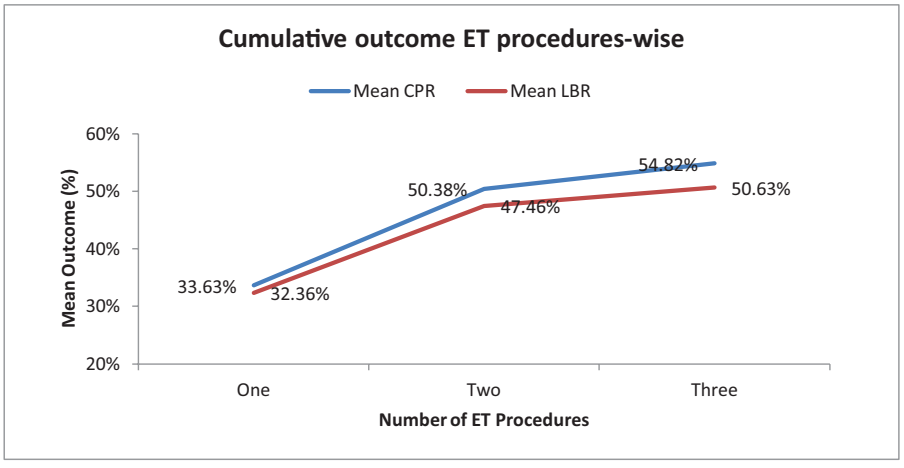

Figure 1: Cumulative outcome of clinical pregnancy rate (CPR) and live-birth rate (LBR) after embryo transfer (ET).

It is evident from the various studies that the female age, body mass index, number of oocytes retrieved, and the quality of embryos influence ART outcomes. We have evaluated the impact of various causes of infertility on CCPR and CLBR.

In our study, we found that in patients with endometriosis, the CCPR and CLBR of 66.67% and 64.10%, respectively, which are higher than the findings of studies by Feichtinger *et al.*[13] (CCPR 42.61% and CLBR 35.56%), Bourdon *et al.*[14] (CCPR 45% and CLBR 31.1%), and Benaglia *et al.*[15] (CCPR 33% and CLBR 25%). All of these studies reported cumulative rates per oocyte retrieval.

Our findings in patients of PCOS suggest CCPR of 58.33% and CLBR 55.83%, whereas the findings by Raymond Li *et al.*[16] and Walls *et al.*[17] reported higher CCPR 62.1% and 65.3%, respectively, but these studies reported CLBR of 50% and 55.1% which are comparable to the findings of our study.

In male factor infertility, CCPR and CLBR reported in our study are 69.41% and 64.71% which are highest among all the diagnostic categories. When compared with other studies, Zacà *et al.*[18] reported a CCPR 37.6% and CLBR 31% in cases of severe OATS. Almekaty *et al.*[19] reported LBR of 15.5% and CLBR of 48.7% after five cycles in cases with nonobstructive azoospermia.

Our findings in female genital tuberculosis suggest a CCPR and CLBR of 37.78% and 35.56%, respectively, which is lesser than that those reported by Lin *et al.*[20] (CCPR 64.6%; CLBR 40.7%).

In our study, we found that CCPR of 29.17% and CLBR of 25% in patients with poor ovarian reserve, whereas a study by Leijdekkers *et al.*[21] reported a CLBR of 56% over multiple cycles. Abdullah *et al.*[22] observed a CLBR after three complete cycles were 77.27%, 42.52%, 51.4%, and 22.34% in POSEIDON 1 to 4, respectively. Bensdorp *et al.*[23] reported a CCPR of 67% and CLBR of 59% after a single oocyte retrieval, whereas findings in our study revealed a CCPR 60.66% and CLBR of 52.46% in cases of unexplained infertility.

The clinical pregnancy and live-birth rates are lowest in women with diminished ovarian reserve and female genital tuberculosis (FGTB). The poor outcome in patients with FGTB is associated with tubal damage, defective endometrium, and due to poor ovarian response.

The extent to which underlying etiology itself can influence ART success rate has been the subject of considerable study. Few studies reported the association between indication for IVF and pregnancy. A study by Bancsi *et al.*[24] evaluated three categories: unexplained infertility, male infertility, and tuboperitoneal disease. Unexplained infertility was considered as the reference category. Women with male infertility or tuboperitoneal disease had lower pregnancy chances compared with those with unexplained infertility. Another study by Ottosen *et al.*[25] reported that women with either male infertility, tubal infertility, or infertility caused by endometriosis had lower pregnancy chances compared with women with unexplained infertility. In the study by Hunault *et al.*,[26] the "indication for IVF" was classified using four categories, with tubal infertility as the reference category. Couples with male infertility or with unexplained infertility had lower pregnancy chances after IVF compared with couples with a tubal factor. The study by Strandell *et al.*[27] reported on each predictor separately. Women with tubal infertility had significantly lower pregnancy chances after IVF and women with the indication endometriosis, male infertility, unexplained infertility, and hormonal factors had higher pregnancy chances though not significant. However, most of the studies in the literature reported that the cause of infertility has no significant effect on outcome of IVF.

Limitations of the study were its retrospective nature and poor prognosis patients were not classified according to POSEIDON criteria.

In the current era of ART practice, our goal is to calculate a meaningful outcome in terms of CLBR per oocyte retrieval to answer a couple's primary question − what is their chance that IVF will result in a baby? The main goal of IVF treatment is to maximize the pregnancy and live-birth rate. Thus frozen-embryo transfer cycles warrant inclusion in estimating CLBR. This also restrains the individuals from physical discomfort and financial burden of repeat cycles. We should try to reduce the burden of the treatment and maximize the outcome of the first complete ART cycle. For future studies, it would be useful to report each indication of IVF as a separate variable instead of combining all indications into one factor, to be able to compare all studies. Cumulative outcomes (per oocyte retrieval) must be classified by specific diagnostic categories, age, and treatment modality to enable the physician to evaluate more accurately the probability of success for patients with specific characteristics.

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Conflicts of interest

There are no conflicts of interest.

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