International Journal of Clinical Obstetrics and Gynaecology

ISSN (P): 2522-6614
ISSN (E): 2522-6622

www.gynaecologyjournal.com
2025;9(3): 154-160
Received: 10-04-2025
Accepted: 12-05-2025

Roya Rozati
MD (A.I.I.M.S, Delhi), F.R.C.O.G. (London), Professor and Head, Dept. of Obst & Gynecology, Shadan Institute of Medical Sciences, Medical and Research Director, Medical Health and Research Institute (MHRI), Hyderabad, Telangana, India

Muhammed Siddique Ahmed khan
Professor HOD, Department of Biochemistry, Shadan Institute of Medical Sciences, Hyderabad, Telangana, India

Abid Ali
Assistant Professor, Bhaskar Medical College, Hyderabad, Telangana, India

Wajeeda Tabasum
M.Sc Genetics, Osmania University, Research Scholar, Medical Health and Research Institute (MHRI), Hyderabad, Telangana, India

Taalia Nazeer Ahmed
M. Pharm, Osmania University, Research Scholar, Medical Health and Research Institute (MHRI), Hyderabad, Telangana, India

Ayapati Gautam Mehdi
Scientist C, Medical Health and Research Institute (MHRI), Hyderabad, Telangana, India

Vikram Aiman Ayapati
Scientist C, Medical Health and Research Institute (MHRI), Hyderabad, Telangana, India

Shamaila Anam
MS, Obstetrics & Gynecology, Shadan Institute of Medical Sciences, Hyderabad, Telangana, India

Corresponding Author:
Roya Rozati
MD (A.I.I.M.S, Delhi), F.R.C.O.G. (London), Professor and Head, Dept. of Obst & Gynecology, Shadan Institute of Medical Sciences, Medical and Research Director, Medical Health and Research Institute (MHRI), Hyderabad, Telangana, India

Ovarian stimulation response and art outcomes among women with different infertility diagnoses undergoing ICSI with embryo pooling

Roya Rozati, Muhammed Siddique Ahmed khan, Abid Ali, Wajeeda Tabasum, Taalia Nazeer Ahmed, Ayapati Gautam Mehdi, Vikram Aiman Ayapati and Shamaila Anam

DOI: https://www.doi.org/10.33545/gynae.2025.v9.i3c.1644

Abstract
Background: Infertility, affecting approximately 10-15% of reproductive-age couples, has multifactorial etiologies including endometriosis, polycystic ovary syndrome (PCOS), tubal factor infertility, male factor infertility, and unexplained infertility. Diminished ovarian reserve (DOR), often associated with poor ovarian response, poses significant challenges in assisted reproductive technology (ART), particularly in intracytoplasmic sperm injection (ICSI) cycles. Embryo pooling has emerged as a potential strategy to improve outcomes in patients with poor response by accumulating viable embryos across multiple stimulation cycles.
Objective: This study aims to evaluate the efficacy of embryo pooling on pregnancy outcomes among women undergoing ICSI across different infertility etiologies, and to assess how these underlying conditions influence ovarian response, oocyte quality, and success rates in both fresh and frozen embryo transfer cycles.
Methods: A retrospective study was conducted involving 220 women undergoing embryo pooling and ICSI at the Medical Health and Research Institute, Hyderabad. Participants were categorized into five etiological groups (n=44 each): endometriosis, PCOS, tubal factor, male factor, and unexplained infertility. Patients were further stratified based on age and AMH levels using the POSEIDON criteria. Ovarian stimulation protocols included GnRH agonist/antagonist, progestin-primed, mild stimulation, or natural cycles. Embryos were cryopreserved and pooled across multiple cycles, with subsequent transfer of one or more embryos based on availability and patient response. The primary outcome was biochemical pregnancy, followed by clinical pregnancy and live birth rates (LBRs).
Results: Ovarian response and oocyte yield varied significantly by infertility etiology. PCOS patients exhibited the highest oocyte yield (≥9 oocytes in 73%), while endometriosis cases were predominantly poor responders (<4 oocytes in 84%). Significant differences were also observed in baseline hormonal profiles and cycle characteristics. In fresh embryo transfers, the highest LBRs were noted in PCOS (46%) and unexplained infertility (43%), while male factor infertility had the lowest (34%). Frozen transfers demonstrated improved outcomes across most groups, with PCOS showing the highest LBR (48%) and CPR (57%). Endometriosis patients also benefited from frozen transfers, suggesting improved endometrial receptivity post-stimulation.
Conclusion: Embryo pooling appears to enhance pregnancy outcomes in women undergoing ICSI, particularly in those with poor ovarian response or advanced reproductive age. Differences in infertility etiology significantly influence ovarian response, oocyte quality, and the effectiveness of fresh versus frozen embryo transfer strategies. Individualized treatment plans guided by the POSEIDON criteria and tailored stimulation protocols may optimize ART success.

Keywords: Endometriosis, PCOS, tubal factor, male infertility, embryo pooling, infertility

Introduction
Infertility affects approximately 10-15% of couples of reproductive age [1] with a range of underlying causes contributing to reproductive challenges. Common etiologies include endometriosis, polycystic ovary syndrome (PCOS), tubal factor infertility, male factor infertility, and unexplained infertility [2]. These etiological factors pose significant challenges to assisted reproductive technologies (ART), as they can adversely impact oocyte retrieval rates, embryo development, and overall pregnancy outcomes [3]. Diminished ovarian reserve (DOR) is characterized by decline in fertility potential resulting from a reduced quantity and quality of

oocytes in women of reproductive age. This condition is commonly attributed to factors such as advanced maternal age, ovarian surgery, cancer therapies, endometriosis, smoking, infections, genetic abnormalities, and environmental influences [4]. They typically produce fewer oocytes, which are often of suboptimal quality. This can result in reduced fertilization rates, impaired embryo development, and ultimately lower probabilities of successful implantation and live birth [5].

Assisted reproductive technologies (ART), particularly intracytoplasmic sperm injection (ICSI), have emerged as effective interventions for a broad range of infertility diagnoses for overcoming certain fertilization barriers, may not fully compensate for the limitations imposed by poor ovarian response [6]. Ovarian reserve is commonly assessed using biochemical and ultrasound-based markers. Elevated basal follicle-stimulating hormone (FSH) levels indicate diminished reserve, while anti-Mullerian hormone (AMH) and antral follicle count (AFC) are considered the most sensitive indicators, reflecting the remaining follicular pool independently of gonadotropic influence [7].

Endometriosis, is characterized by the ectopic implantation of endometrial-like tissue outside the uterine cavity, is commonly linked to adverse outcomes in assisted reproductive technology (ART). The condition induces chronic pelvic inflammation and oxidative stress, often leading to disrupted pelvic anatomy and compromised folliculogenesis [8]. As a result, women with endometriosis typically demonstrate a reduced ovarian response during controlled ovarian stimulation (COS) for intracytoplasmic sperm injection (ICSI), due to both diminished ovarian reserve and impaired oocyte quality [9]. Surgical intervention for endometriomas may further exacerbate this response by reducing functional ovarian tissue [10].

Polycystic ovary syndrome (PCOS), a common endocrine disorder, is often associated with an exaggerated ovarian response during controlled ovarian stimulation (COS) for intracytoplasmic sperm injection (ICSI), largely due to elevated antral follicle count and anti-Müllerian hormone (AMH) levels indicating preserved ovarian reserve [11]. However, oocyte maturation and quality may be compromised by metabolic and hormonal disturbances, such as hyperandrogenism and insulin resistance. These factors can also impair endometrial receptivity, potentially diminishing implantation and pregnancy outcome [12].

Tubal factor infertility, caused by structural damage or blockage of the fallopian tubes from infections, surgery, or endometriosis, is a common indication for assisted reproductive technology (ART) [13]. Ovarian reserve and endocrine function typically remain intact, allowing a normal ovarian response during controlled ovarian stimulation (COS) for intracytoplasmic sperm injection (ICSI). However, pelvic adhesions or hydrosalpinx can impair implantation and pregnancy rates, particularly due to inflammatory fluid affecting the uterine environment. Surgical removal of hydrosalpinx prior to embryo transfer has been shown to improve ART outcomes [14].

Male factor infertility primarily involves alterations in semen quality, including sperm concentration, motility, or morphology, without directly impacting the female partner's reproductive physiology. Nevertheless, it necessitates targeted interventions within assisted reproductive technologies.

In unexplained infertility women typically exhibit normal ovarian reserve and endocrine function, leading to a standard response to controlled ovarian stimulation (COS) during intracytoplasmic sperm injection (ICSI) [15]. Although oocyte yield and embryo quality are often comparable to those seen in other infertility etiologies, underlying subtle abnormalities such as impaired gamete interaction, undetected endometrial dysfunction, or early embryonic developmental defects-may contribute to infertility. The absence of identifiable causes following normal assessments of ovulation, tubal patency, and semen parameters, despite prolonged failure to conceive.

The heterogeneity in pathophysiology across these etiologies is reflected in variable responses to controlled ovarian stimulation (COS), oocyte yield and maturation, and embryo transfer outcomes. Fresh versus frozen embryo transfer strategies may also differentially impact success rates depending on the infertility diagnosis, due to differences in hormonal environment and endometrial receptivity [16].

To better stratify and individualize ART strategies for women with poor ovarian response, the POSEIDON (Patient-Oriented Strategies Encompassing Individualized Oocyte Number) classification was introduced. This categorizes patients based on age, ovarian biomarkers (AMH and AFC), and prior ovarian response, enabling clinicians to tailor treatment protocols more precisely [17]. One emerging strategy for women classified under the low prognosis POSEIDON groups is embryo pooling, where multiple stimulation cycles are performed to accumulate an adequate number of embryos for transfer. Embryo pooling, which involves the sequential accumulation and cryopreservation of embryos obtained from multiple controlled ovarian stimulation (COS) cycles, has emerged as a strategic approach to address these limitations. By increasing the total number of embryos available for selection and transfer, this method may enhance the likelihood of achieving a viable pregnancy, particularly in women with low ovarian reserve or those of advanced reproductive age. This approach aims to improve the cumulative pregnancy rate in patients with low oocyte yield in single cycles. Therefore, this study aims to evaluate the efficacy of embryo pooling in improving pregnancy outcomes with different etiologies in women undergoing ICSI, and to evaluate how these factors influence ovarian response, oocyte quality, and pregnancy outcomes in both fresh and frozen embryo transfer cycles.

Materials and Methods

A retrospective study was conducted at the Medical Health and Research Institute, Hyderabad, involving 220 women who underwent embryo pooling from March 2022 to March 2025. Participants were categorized according to the POSEIDON criteria and stratified into four groups based on Age and anti-Mullerian hormone (AMH) levels-below and above 1.2 ng/mL. Institutional Ethical approval was obtained, and informed consent was taken from all participants. The primary outcome measure was biochemical pregnancy, determined by positive β-hCG following embryo transfer. Clinical pregnancy outcomes were subsequently assessed.

Patients were counseled for embryo pooling after reviewing the reports of AMH and were counseled about second and third ovarian stimulation when less than two grade A cleavage stage embryos will be formed after the first stimulation cycle. Patients were counseled for embryo pooling based on their AMH levels. Those with fewer than two Grades A cleavage-stage embryos after the first stimulation cycle were advised on the need for a second or third ovarian stimulation.

In the embryo pooling group, all couples were offered several consecutive stimulating cycles until accumulate at least three to five embryos to be transferred. Embryos were thawed prior to transfer, with one or more embryos transferred per cycle until a successful pregnancy was achieved or all embryos were utilized.

Ovarian stimulation was initiated using a GnRH

agonist/antagonist protocol, progestin-primed ovarian stimulation (PPOS), mild stimulation, or a natural cycle, as determined by the clinician. In the long protocol, a GnRH analogue (GnRHa) was administered for pituitary desensitization. On days 2-3 of the menstrual cycle, Transvaginal ultrasound and serum estradiol measurements were performed. Human menopausal gonadotropin (hMG) or recombinant FSH (rFSH) was administered at 225-300 IU per day, with dosage adjustments based on Antral follicle count (AFC), patient age, body mass index (BMI), and prior ovarian response. Ovarian response was monitored via serial Transvaginal ultrasound, with or without hormonal assessment, and further dosage modifications. In the antagonist protocol, 0.25 mg of cetrorelix was administered daily from the sixth day of stimulation until ovulation trigger. In the PPOS protocol, Medroxyprogesterone acetate (MPA, 10 mg/day) was given concurrently with ovarian stimulation. Mild stimulation involved clomiphene citrate (100 mg for 5 days), followed by hMG (150 IU/day) until ovulation trigger. Final oocyte maturation was induced when follicles reached ≥18 mm in diameter using triptorelin (0.1 mg) and hCG (2000 IU) or Ovidrel (250 µg). Oocyte retrieval was performed approximately 36 hours post-trigger.

Fertilization and embryo evaluation

Approximately 2 hours post-oocyte retrieval, each oocyte was inseminated with motile spermatozoa. Following insemination, oocytes were denuded and assessed for the presence of two pronuclei to confirm fertilization. Embryo quality was evaluated on day 3 based on blastomere symmetry and degree of fragmentation, and graded from Grade 1 to Grade 6. Embryos of 6-8 cells and of grade one or two were regarded as top-quality embryos were placed in extended culture until they reached the blastocyst stage.

Patients who did not achieve pregnancy in the stimulated IVF cycle or opted to postpone fresh transfer underwent frozen embryo transfer (FET) at least two months later. Only embryos with over 50% intact blastomeres after thawing were selected for transfer. FET was performed in natural cycles for ovulatory women, while anovulatory women underwent clomiphene-induced or hormonal preparation.A maximum of two embryos or blastocysts were transferred per frozen embryo transfer (FET) cycle.

Results

A total of 220 patients undergoing intracytoplasmic sperm injection (ICSI) were evenly distributed across five infertility etiologies: endometriosis, polycystic ovary syndrome (PCOS), tubal factor, male infertility, and unexplained infertility (n=44 per group). Across all categories, the majority of patients underwent a single ICSI cycle (73%-86%), while a smaller proportion required 2-3 cycles (11%-20%) or ≥4 cycles (2%-5%). Oocyte yield varied notably by etiology. Patients with endometriosis were predominantly poor responders, with 84% retrieving fewer than 4 oocytes. In contrast, those with PCOS demonstrated a robust ovarian response, with 73% retrieving ≥9 oocytes. Tubal factor infertility was associated with a moderate response, where 70% retrieved 4-9 oocytes and 14% ≥9 oocytes. Among male infertility cases, 57% had 4-9 oocytes retrieved, while 18% had ≥9. In unexplained infertility, 55% retrieved 4-9 oocytes and 32% retrieved fewer than 4, indicating variable ovarian responsiveness across etiologies, as depicted in Flow Chart 1.

The table 1 presents the baseline characteristics of 220 infertile couples undergoing intracytoplasmic sperm injection (ICSI), categorized into five etiological groups: endometriosis (n=44), polycystic ovary syndrome (PCOS) (n=44), tubal factor infertility (n=44), male factor infertility (n=44), and unexplained infertility (n=44).

The mean age of participants ranged from 27.53±3.82 years in the endometriosis group to 31±5.8 years in the unexplained infertility group, with a statistically significant difference observed between groups ($P = 0.05$). Body mass index (BMI) was significantly higher in the PCOS group (28.2±3.1 kg/m²) compared to other groups ($P = 0.001$).

Regarding infertility type, primary infertility was most prevalent among couples with unexplained infertility (72.7%), while secondary infertility was more common in the PCOS and tubal factor groups.

The mean duration of infertility varied from 5.13±2.82 years in the unexplained infertility group to 7.42±3.2 years in the PCOS group ($P = 0.05$).

Baseline hormonal profiles also showed significant intergroup differences. The PCOS group exhibited the lowest mean FSH levels (4.14±1.58 mIU/mL) and the highest LH levels (8.92±5.46 mIU/mL), both statistically significant ($P < 0.001$ and $P = 0.004$, respectively). Estradiol levels were significantly elevated in all groups, with the highest mean level observed in the tubal factor group (3,721.9±1,847.2 pg/mL; $P < 0.001$).

Anti-Müllerian hormone (AMH) levels were significantly elevated in the PCOS group (7.34±3.73 ng/mL) compared to others ($P < 0.001$), correlating with the highest antral follicle count (AFC: 14.5±3.2; $P < 0.001$).

Semen parameters also varied significantly. The highest sperm concentration and motility were observed in the unexplained infertility group (52.8±12.7 ×10⁶/mL and 53.4±11.6%, respectively), whereas the lowest values were noted in the endometriosis group (36.5±26.8 ×10⁶/mL and 4.02±3.3%, respectively) ($P < 0.001$).

The distribution of treatment cycles across various infertility groups was analyzed. For individuals with endometriosis, the majority (72.7%) underwent only one cycle, while 22.7% required 2-3 cycles, and a smaller proportion (4.6%) underwent four or more cycles. Similarly, polycystic ovary syndrome (PCOS) was predominantly associated with one treatment cycle (86.4%), with 11.4% undergoing 2-3 cycles and only 2.2% requiring ≥4 cycles. In the tubal factor infertility group, 79.5% underwent a single cycle, 15.9% needed 2-3 cycles, and 4.6% required multiple cycles. For male factor infertility, 81.8% completed only one cycle, 13.6% underwent 2-3 cycles, and 4.6% had ≥4 cycles. Lastly, individuals with unexplained infertility showed a similar pattern, with 75% completing one cycle, 20.5% undergoing 2-3 cycles, and 4.6% needing ≥4 cycles (Figure 1). These data suggest that most patients across all infertility groups tend to complete a single treatment cycle, with a progressively smaller proportion requiring additional cycles in Table 2

The table 3 presents the outcomes of ovarian stimulation cycles in patients undergoing Intracytoplasmic Sperm Injection (ICSI), stratified by different infertility diagnoses: Endometriosis, PCOS, Tubal Factor Infertility, Male Factor Infertility, and Unexplained Infertility. Key parameters evaluated include the mean number of oocytes retrieved, metaphase II (MII) oocytes, metaphase I (MI) oocytes, and germinal vesicle (GV) oocytes. Additionally, the distribution of oocyte retrievals into three categories (<4, 4-9, and ≥9 oocytes) is provided in Figure 2. Statistical analysis indicates significant differences in oocyte yield and maturation across diagnoses, with PCOS patients

showing the highest oocyte retrieval and Endometriosis patients yielding the fewest oocytes. This underscores the impact of infertility etiology on ovarian response and oocyte quality during stimulation cycles, emphasizing the need for tailored stimulation protocols to optimize ICSI outcomes.

In fresh embryo transfers, the highest LBR was observed in patients with PCOS (46%), followed closely by those with unexplained infertility (43%), tubal factor infertility (42%), and endometriosis (41%). The lowest LBR was seen in male factor infertility cases (34%). Similarly, CPRs in the fresh cycle were highest in the PCOS group (52%), followed by tubal factor infertility (48%), male factor infertility (47%), unexplained infertility (47%), and endometriosis (46%).

In frozen embryo transfers, an overall improvement in outcomes was noted for most groups. The PCOS group maintained the highest LBR (48%) and CPR (57%), indicating enhanced clinical success with deferred embryo transfer. Tubal factor infertility also showed strong outcomes, with an LBR of 46% and CPR of 52%. Patients with endometriosis exhibited improved results in the frozen cycle (LBR: 44%, CPR: 51%) compared to the fresh cycle, suggesting a potential benefit from endometrial recovery before embryo transfer. Unexplained infertility had stable LBR (41%) and CPR (45%) across both cycles. In contrast, male factor infertility demonstrated a moderate increase in CPR (54%) during frozen cycles, although LBR (37%) remained lower than in other groups as depicted in Table 4.

Discussion

Our Study provides a comprehensive comparison of clinical, hormonal, and oocyte retrieval outcomes were observed in 220 patients undergoing intracytoplasmic sperm injection (ICSI) across five major infertility etiologies Endometriosis, pcos, Tubal factor, male infertility and unexplained Infertility.

Our study has significant variability in ovarian response and baseline characteristics, underscoring the importance of etiology-specific approaches in assisted reproductive technologies (ART).

PCOS patients has shown the highest ovarian response, with 73% retrieving ≥9 oocytes, likely attributable to elevated serum AMH levels and AFC, along with lower baseline FSH indicators of high ovarian reserve in PCOS and are subjected to Ovarian Hyperstimulation syndrome and are consistent with previous literature describing excessive follicular recruitment and multifollicular development in these patients [18]. Furthermore, both live birth rate (LBR) and clinical pregnancy rate (CPR) were highest in this group, especially in frozen embryo transfers, aligning with growing evidence that frozen cycles may improve outcomes in PCOS by reducing the risk of OHSS and enhancing endometrial receptivity [19, 20].

In patients with endometriosis showed significantly lower oocyte yield, with 84% retrieving fewer than four oocytes, suggesting a poor ovarian response. This diminished response could be linked to the inflammatory nature of endometriosis and prior surgical interventions, which are known to reduce ovarian reserve [21]. However, an improvement in CPR (51%) and LBR (44%) during frozen cycles indicates potential benefits of allowing endometrial recovery before embryo transfer, which has also been supported by studies advocating deferred transfer in such patients [22].

Tubal factor infertility patients exhibited a moderate ovarian response and favorable outcomes in both fresh and frozen transfers. This is expected, as the underlying etiology generally does not impair ovarian reserve or endocrine function. These patients had relatively high LBRs (42%-46%) and CPRs (48%-52%).

In male factor infertility, although female partners displayed reasonable ovarian responses, live birth outcomes were comparatively lower, particularly in fresh cycles (LBR: 34%). This suggests that sperm quality, despite ICSI, can still influence embryo viability and implantation [23]. Interestingly, CPR improved in frozen cycles (54%), which may indicate better synchrony between embryo and endometrium in hormone-controlled environments, although the LBR remained modest (37%).

Table 1: Socio-Demographic baseline characteristics of infertile couples undergoing ICSI

Total Number Subjects (n=220)	Endometriosis (n=44)	PCOS (n=44)	Tubal factor (n=44)	Male Infertility (n=44)	Unexplained Infertility (n=44)	P-Value
Age	27.53±3.82	28.6±4.7	29.8.0±3.3	30.2±6.1	31±5.8	0.05*
BMI	23.11±3.51	28.2±3.1	27.8±4.9	27.1±5.8	26.9±6.2	0.001*
Infertility type						
Primary	26(59.09)	20(45.4)	19(43.1)	28(63.6)	32(72.7)	
Secondary	18(40.9)	24(54.5)	25(56.8)	16(36.3)	12(27.2)	
Duration of infertility (years)	6.99±3.67	7.42±3.2	6.72±4.42	5.62±2.72	5.13±2.82	0.05*
Basal serum FSH (mIU/mL)	6.12±3.72	4.14±1.58	6.38±2.01	6.7±2.3	6.47±1.8	<0.001*
Basal serum LH level (mIU/mL)	6.24±2.26	8.92±5.46	5.92±1.44	7.52±2.72	6.92±2.72	0.004*
Basal serum E2 level (pg/mL)	1,562.4±1057.3	3,219.2±1,747.2	3,721.9±1,847.2	3,576.1±1,890.2	3,233.9±1,488.0	<0.001*
Serum AMH(ng/ml)	1.52±1.91	7.34±3.73	1.81±1.32	2.42±1.61	2.6±1.91	<0.001*
Antral Follicle Count	7.32±3.21	14.5±3.2	11.2±3.5	12.6±3.8	11.2±6.8	<0.001*
Sperm concentration ($\times 10^6$ /mL)	36.5±26.8	42.4±6.8	29.5±11.9	31±14.4	52.8±12.7	<0.001*
Sperm motility (%)	4.0.2±3.3	46.8±7.2	41.8±5.2	42.4±1.2	53.4±11.6	<0.001*

Unexplained infertility represents a heterogeneous category where no definitive pathology is identified. As expected, the variability in ovarian response and clinical outcomes was moderate and consistent across both fresh and frozen cycles. This group had a stable LBR (43% fresh vs. 41% frozen) and CPR (47% vs. 45%), aligning with the literature suggesting that undiagnosed subtle factors, such as impaired oocyte competence or endometrial receptivity, might limit treatment success [24].

The small proportion requiring multiple cycles may reflect either suboptimal outcomes in the first attempt or physician preference for additional cycles to improve cumulative success rates. Overall, the study emphasizes the importance of individualized treatment strategies in ICSI. Recognizing the distinct pathophysiological mechanisms and clinical profiles associated with each infertility diagnosis can guide more effective ovarian stimulation protocols, enhance oocyte yield, and ultimately

improve reproductive outcomes. The outcomes of ICSI vary substantially based on the underlying infertility diagnosis. Frozen embryo transfers appear particularly beneficial in conditions like PCOS and endometriosis, likely due to improved endometrial conditions and reduced risk of OHSS.

Diminished ovarian reserve (DOR) is affected by multiple factors, including lifestyle choices such as smoking, medical conditions like endometriosis, and iatrogenic causes such as chemotherapy or ovarian surgery. Additionally, autoimmune disorders and environmental factors contribute to its development. Emerging evidence suggests that oxidative stress, hypoxia, and vitamin D deficiency play a significant role in the pathogenesis of DOR.

Table 2: Depicts the Distribution of Infertility Treatment Cycles by Diagnosis

Infertility Group	Only 1 Cycle (n, %)	2-3 cycles	≥ 4 Cycles
Endometriosis	32(72.7%)	10(22.7%)	2(4.6%)
PCOS	38(86.4%)	5(11.4%)	1 (2.2%)
Tubal factor	35(79.5%)	7(15.9%)	2(4.6%)
Male factor	36(81.8%)	6(13.6%)	2(4.6%)
Unexplained Infertility	33(75%)	9(20.5%)	2(4.6%)

Table 3: Oocyte Retrieval Outcomes after Ovarian Stimulation across Infertility Diagnoses

Infertility Diagnosis	Mean Oocytes Retrieved (Mean ±SD)	MII (Mean ±SD)	MI (Mean ±SD)	GV (Mean ±SD)	<4 Oocytes (n, %)	4-9 Oocytes (n, %)	≥9 Oocytes (n, %)	P-Value
Endometriosis (n=44)	12.91±11.34	9±7.6	1.4±2.03	2.01±3	37 (84%)	5 (11.3%)	2 (4.5%)	0.032
PCOS (n=44)	16.82±8.42	12.1±6.62	2.68±1.75	3.02±2.4	5 (11.3%)	7 (15.9%)	32 (72.7%)	0.032
Tubal Factor Infertility (n=44)	12.32±5.41	8.42±4.21	2.32±1.28	3.08±3.34	7 (15.9%)	31 (22.7%)	6 (13.6%)	0.032
Male Factor Infertility (n=44)	11.02±4.26	8.44±4.62	1.9±2.02	2.08±3	11 (25%)	25 (56.8%)	8 (18.1%)	0.012
Unexplained Infertility (n=44)	12.05±4.26	8.2±3.4	1.1±2.4	1.98±2.1	14 (31.8%)	24 (54.5%)	6 (13.6%)	0.308

Table 4: Represents Clinical Outcomes of Fresh and Frozen Embryo Transfers in Patients with different indications

Infertility Diagnosis	Endometriosis (n=44)	PCOS (n=44)	Tubal Factor (n=44)	Male Factor Infertility (n=44)	Unexplained Infertility (n=44)
Fresh					
LBR	41%	46%	42%	34%	43%
CPR	46%	52%	48%	47%	47%
Frozen					
Live birth rate	44%	48%	46%	37%	41%
CPR	51%	57%	52%	54%	45%

Flowchart 1: Depicts the Distribution of ICSI Patients by Infertility Diagnosis, Treatment Cycles, and Oocyte Retrieval Outcomes

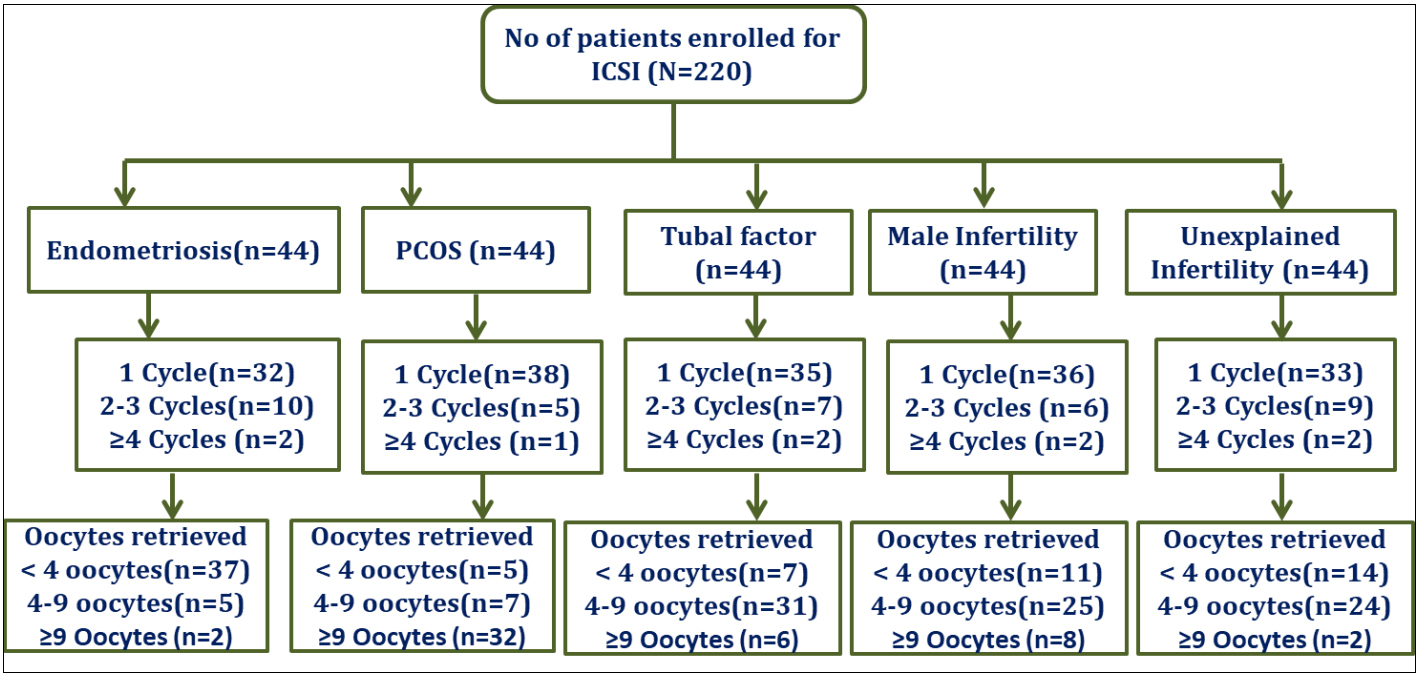

Fig 1: Represents Number of ICSI cycles across Infertility groups

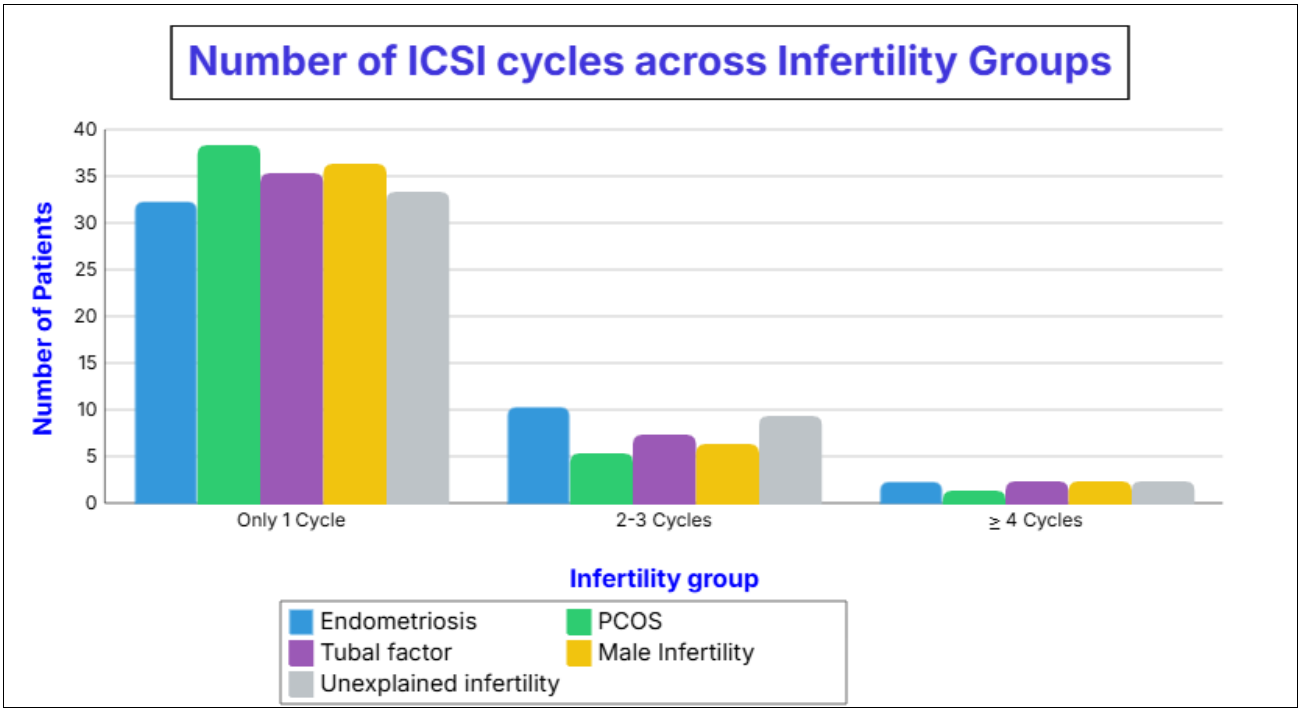

Fig 2: Represents Oocyte retrieval after Ovarian Stimulation across Infertility Groups

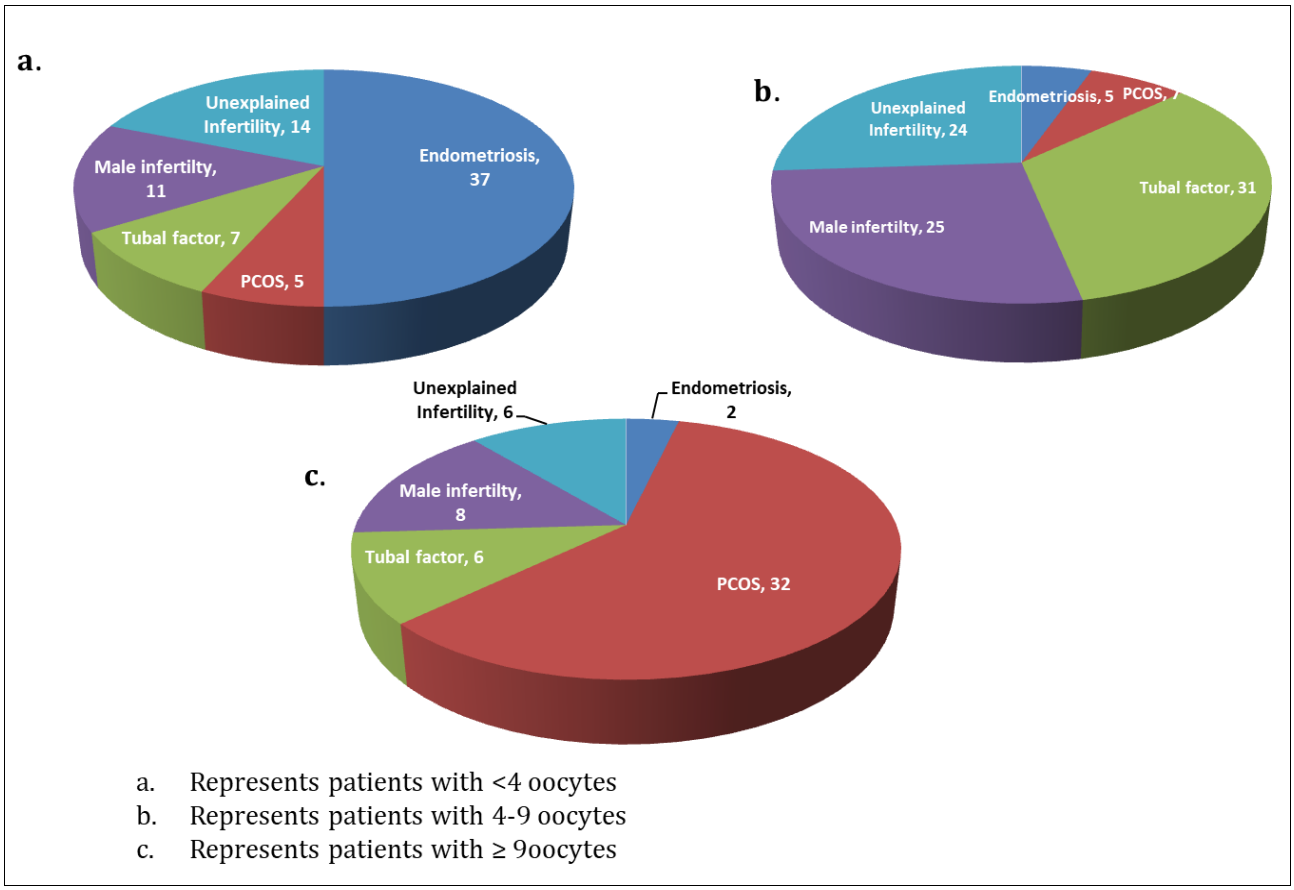

Fig 3: Oocyte retrieval outcomes after ovarian stimulation across infertility diagnosis

Conclusion

Our study provides the significant influence of infertility etiology on ovarian response, oocyte quality, and pregnancy outcomes in women undergoing intracytoplasmic sperm injection (ICSI) with embryo pooling strategies. Our findings demonstrate marked variability in clinical, hormonal, and embryological parameters across five common infertility diagnoses—endometriosis, polycystic ovary syndrome (PCOS), tubal factor, male factor, and unexplained infertility. Women with PCOS exhibited the highest ovarian reserve, oocyte yield, and clinical success rates, particularly in frozen embryo transfer cycles, supporting the benefits of deferred transfer in mitigating risks like OHSS and enhancing endometrial receptivity. Conversely, patients with endometriosis had the poorest ovarian

response, yet still benefited from frozen embryo transfers, likely due to improved endometrial conditions after recovery from controlled ovarian stimulation. Tubal factor infertility was associated with consistent and favorable outcomes, reflecting intact ovarian function despite structural reproductive tract abnormalities. Male factor infertility presented with modest reproductive outcomes, suggesting that sperm quality, even when circumvented via ICSI, may still impact embryo development and implantation potential. In unexplained infertility, the heterogeneity of underlying pathophysiology led to variable but overall moderate outcomes across treatment modalities.

Embryo pooling emerged as a promising approach to improve cumulative pregnancy rates, particularly in patients with low oocyte yield or diminished ovarian reserve. The data support the use of individualized ovarian stimulation protocols and strategic embryo transfer timing, especially in POSEIDON-classified low-prognosis groups.

In conclusion, our findings reinforce the importance of individualized assisted reproductive strategies tailored to the specific infertility diagnosis, age, and ovarian reserve profile of each patient which enhances clinical outcomes. Integration of embryo pooling and personalized timing of embryo transfer—especially via frozen cycles—can optimize reproductive outcomes and improve the management of subfertile couples across diverse clinical presentations.

Funding

This study was funded by Indian Council of Medical Research.

Conflict of interest

All authors declare that they have no conflict of interest.

Acknowledgement

We acknowledge all the authors of the manuscript.

References

1. Luo Y, Hong C, Fan H, *et al*. Trends and distribution of infertility—Asia Pacific region, 1990-2021. China CDC Weekly. 2024 Jul 12;6(28):689.
2. Carson SA, Kallen AN. Diagnosis and management of infertility: a review. JAMA. 2021 Jul 6;326(1):65-76.
3. Broekmans FJ, Kwee J, Hendriks DJ, *et al*. A systematic review of tests predicting ovarian reserve and IVF outcome. Human Reproduction Update. 2006 Nov;12(6):685-718.
4. Cohen J, Chabbert-Buffet N, Darai E. Diminished ovarian reserve, premature ovarian failure, poor ovarian responder—a plea for universal definitions. Journal of Assisted Reproduction and Genetics. 2015 Dec;32:1709-1712.
5. Feng K, Zhang Z, Wu L, *et al*. Predictive factors for the formation of viable embryos in subfertile patients with diminished ovarian reserve: a clinical prediction study. Reproductive Sciences. 2024 Jun;31(6):1747-1756.
6. Ashourzadeh S, Safari S, Hosseinisadat R, *et al*. Comparative analysis of conventional *in vitro* fertilization and intracytoplasmic sperm injection in patients with polycystic ovarian syndrome, tubal factor infertility, and unexplained infertility whose partners exhibit normal semen parameters: a retrospective study of sibling oocytes. Clinical and Experimental Reproductive Medicine. 2024 Mar 25;51(4):285.
7. Deadmond A, Koch CA, Parry JP. Ovarian reserve testing. Endotext [Internet]. 2022 Dec 21.
8. Lin YH, Chen YH, Chang HY, *et al*. Chronic niche inflammation in endometriosis-associated infertility: current understanding and future therapeutic strategies. International Journal of Molecular Sciences. 2018 Aug 13;19(8):2385.
9. Findikli N, Janssens S, Fasano G, *et al*. The effects of endometriosis on oocyte and embryo quality. Journal of Clinical Medicine. 2025 Mar 28;14(7):2339.
10. Bonavina G, Taylor HS. Endometriosis-associated infertility: from pathophysiology to tailored treatment. Frontiers in Endocrinology. 2022 Oct 26;13:1020827.
11. Rudnicka E, Kunicki M, Calik-Ksepka A, *et al*. Anti-Müllerian hormone in pathogenesis, diagnostic and treatment of PCOS. International Journal of Molecular Sciences. 2021 Nov 19;22(22):12507.
12. Singh S, Pal N, Shubham S, *et al*. Polycystic ovary syndrome: etiology, current management, and future therapeutics. Journal of Clinical Medicine. 2023 Feb 11;12(4):1454.
13. Shen H, Cai M, Chen T, *et al*. Factors affecting the success of fallopian tube recanalization in treatment of tubal obstructive infertility. Journal of International Medical Research. 2020 Dec;48(12):0300060520979218.
14. Melo P, Georgiou EX, Johnson N, *et al*. Surgical treatment for tubal disease in women due to undergo *in vitro* fertilisation. Cochrane Database of Systematic Reviews. 2020;(10).
15. Chen J, Liu L, Liu Z, *et al*. Intracytoplasmic sperm injection hampers fertilization rate and pregnancy per initiated cycle in patients with extremely poor ovarian response. Archives of Gynecology and Obstetrics. 2025 Apr 30:1-9.
16. Han Y, Liu C, Liu D, *et al*. Pregnancy outcomes in freeze-all versus fresh embryo transfer cycles of women with adenomyosis and endometriosis: a systematic review and meta-analysis. Frontiers in Endocrinology. 2025 May 14;16:1507252.
17. Roque M, Sunkara SK. The most appropriate indicators of successful ovarian stimulation. Reproductive Biology and Endocrinology. 2025 Jan 9;23(Suppl 1):5.
18. Salemi F, Jambarsang S, Kheirkhah A, *et al*. The best ovarian reserve marker to predict ovarian response following controlled ovarian hyperstimulation: a systematic review and meta-analysis. Systematic Reviews. 2024 Dec 18;13(1):303.
19. Okohue JE, Onuh SO, Ikimalo JI. Comparison of IVF/ICSI outcome in patients with polycystic ovarian syndrome or tubal factor infertility. Nigerian Journal of Clinical Practice. 2013 May 27;16(2):207-210.
20. Chen ZJ, Shi Y, Sun Y, *et al*. Fresh versus frozen embryos for infertility in the polycystic ovary syndrome. New England Journal of Medicine. 2016 Aug 11;375(6):523-533.
21. Li A, Zhang J, Kuang Y, *et al*. Analysis of IVF/ICSI-FET outcomes in women with advanced endometriosis: influence on ovarian response and oocyte competence. Frontiers in Endocrinology. 2020 Jul 17;11:427.
22. Vidales LM, Lawrenz B, Vitorino RL, *et al*. Clinical and laboratory parameters associated with cycle outcomes in patients undergoing euploid frozen blastocyst transfer. Reproductive BioMedicine Online. 2023 Jun 1;46(6):917-925.
23. Esteves SC, Roque M, Bedoschi G, *et al*. Intracytoplasmic sperm injection for male infertility and consequences for offspring. Nature Reviews Urology. 2018 Sep;15(9):535-562.
24. Shingshetty L, Maheshwari A, McLernon DJ, *et al*. Should we adopt a prognosis-based approach to unexplained infertility?. Human Reproduction Open. 2022 Jan 1;2022(4):hoac046.