Original Article

Analysing Maternal and Neonatal Outcomes of IVF/ICSI Conceived Pregnancies with Spontaneous Conceived Pregnancies

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Abstract

Background: The use of Assisted Reproductive Technology (ART), particularly In Vitro Fertilization (IVF) and Intracytoplasmic Sperm Injection (ICSI), has increased globally. While successful in treating infertility, concerns persist regarding potential adverse maternal and neonatal outcomes compared to spontaneously conceived (SC) pregnancies. This study aimed to prospectively analyse and compare these outcomes in a North Indian population. **Material and Methods:** This prospective observational study was conducted over one year at a tertiary care centre in Kanpur. A total of 100 pregnant women were enrolled and divided into two groups: 50 women who conceived through IVF/ICSI (Study Group) and 50 women who conceived spontaneously (Control Group). Participants were singleton pregnancies and were followed from the first trimester until delivery. Data on baseline demographics, maternal complications, and neonatal outcomes were collected. Statistical analysis was performed using Student's t-test for continuous variables and the Chi-square test for categorical variables. A p-value <0.05 was considered statistically significant. **Results:** The mean maternal age was significantly higher in the IVF/ICSI group (32.4 ± 4.1 years) compared to the SC group (28.1 ± 3.5 years) (p<0.001). The IVF/ICSI group had a significantly higher incidence of gestational diabetes mellitus (20% vs. 8%, p=0.041), pre-eclampsia (16% vs. 6%, p=0.035), and Caesarean section (62% vs. 34%, p=0.003). Neonates in the IVF/ICSI group had a lower mean gestational age at birth (38.2 ± 1.5 weeks vs. 39.1 ± 1.1 weeks, p<0.001) and lower mean birth weight (2.9 ± 0.4 kg vs. 3.2 ± 0.3 kg, p<0.001). Consequently, rates of preterm birth (20% vs. 6%, p=0.027) and NICU admission (22% vs. 8%, p=0.031) were significantly higher in the study group. **Conclusion:** Pregnancies conceived via IVF/ICSI are associated with a higher risk of adverse maternal and neonatal outcomes compared to spontaneous conceptions. This increased risk may be multifactorial, stemming from underlying parental factors and the ART procedures themselves. These findings underscore the need for heightened antenatal surveillance and specialized care for this high-risk obstetric population.

Keywords: Assisted Reproductive Technology, IVF, ICSI, Maternal Outcome, Neonatal Outcome, Preterm Birth, Pre-eclampsia.

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Introduction

The advent of Assisted Reproductive Technology (ART) has revolutionized the management of infertility, enabling millions of couples worldwide to achieve parenthood.[1] In Vitro Fertilization (IVF) and Intracytoplasmic Sperm Injection (ICSI) are the cornerstones of modern ART, with their utilization showing a consistent upward trend globally, including in India.[2] While the primary goal of ART is a healthy live birth, the journey from conception to delivery is often complex. An accumulating body of evidence suggests that pregnancies conceived through ART may be associated with a higher risk of adverse perinatal outcomes compared to those conceived spontaneously.[3]

Maternal complications reportedly increased in ART pregnancies include hypertensive disorders of pregnancy, such as pre-eclampsia and gestational hypertension, as well as gestational diabetes mellitus (GDM) and placenta previa.[4,5] Furthermore, a significantly higher rate of Caesarean section is consistently observed in the ART population, which may be partly due to medical indications and partly due to elective decisions influenced by the "precious baby" phenomenon.[6]

From a neonatal perspective, a major concern is the increased risk of preterm birth (PTB) and low birth weight (LBW) among ART-conceived infants, even in singleton pregnancies.[7] These outcomes are significant contributors to neonatal morbidity and mortality and can have long-term health implications, including neurodevelopmental delays and chronic diseases in later life.[8] The reasons for these disparities are debated and likely multifactorial. It remains a challenge to disentangle the effects of the ART procedures themselves (e.g., ovarian hyperstimulation, in vitro culture, embryo manipulation) from the underlying parental factors that led to infertility (e.g., advanced maternal age, polycystic ovary syndrome, endometriosis, poor sperm quality).[9] Several recent large-scale registry studies and meta-

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analyses have confirmed these associations, but data from specific geographic and ethnic populations remain limited.[10] Regional variations in clinical practice, patient demographics, and healthcare systems can influence outcomes, highlighting the need for local data. In the Indian context, where ART clinics are rapidly proliferating, there is a research gap for prospective studies that meticulously follow pregnancies from conception to delivery to provide robust, region-specific evidence.

Therefore, this prospective study was designed with the primary aim to analyse and compare maternal and neonatal outcomes in a cohort of singleton pregnancies conceived via IVF/ICSI versus those conceived spontaneously at a tertiary care hospital in Kanpur, India.

Materials and Methods

Study Design and Setting: This was a prospective, observational, comparative study conducted in the Department of Obstetrics and Gynaecology at Rama Medical College, Kanpur, over a period of 12 months (from January 2023 to December 2023).

Sample Size and Sampling: A total of 100 pregnant women were enrolled. Using convenience sampling, they were allocated into two groups:

- Study Group: 50 women with singleton pregnancies conceived through IVF/ICSI.
- Control Group: 50 women with singleton pregnancies conceived spontaneously, who were matched for booking at a similar gestational age.

Inclusion Criteria

1. Pregnant women aged 21–40 years.
2. Confirmed singleton pregnancy on first-trimester ultrasound.
3. Willingness to participate and provide written informed consent.
4. Booked for antenatal care at the study hospital before 14 weeks of gestation.

Exclusion Criteria

1. Multiple pregnancies (twins or higher-order).
2. Pre-existing chronic medical conditions (e.g., chronic hypertension, pre-gestational diabetes, renal disease, autoimmune disorders).
3. Pregnancies conceived through ovulation induction with timed intercourse or Intrauterine Insemination (IUI).
4. Known uterine anomalies or significant fibroids.

Study Procedure: Upon recruitment, a detailed history was taken, including demographic information, obstetric history, and details of the current conception. For the study group, specifics of the ART cycle were noted. All participants underwent standard antenatal care as per hospital protocol.

Maternal outcomes were monitored throughout the pregnancy. This included screening for GDM with a 75g oral glucose tolerance test (OGTT) between 24–28 weeks and regular monitoring of blood pressure to screen for hypertensive disorders. The development of pre-eclampsia (defined as new-onset hypertension after 20 weeks with proteinuria or end-organ dysfunction), GDM, and other complications were recorded. The mode of delivery (vaginal or Caesarean section) and its indication were documented.

Neonatal outcomes were assessed immediately after birth. Data collected included gestational age at birth (calculated from the last menstrual period for the SC group and from the date of oocyte retrieval/embryo transfer for the IVF/ICSI group), birth weight, Apgar scores at 1 and 5 minutes, and the need for admission to the Neonatal Intensive Care Unit (NICU). Preterm birth was defined as delivery before 37 completed weeks of gestation, and low birth weight was defined as a birth weight of less than 2500 grams.

Statistical Analysis: Data were entered into a Microsoft Excel spreadsheet and analysed using the Statistical Package for the Social Sciences (SPSS) version 25.0. Continuous variables were expressed as mean ± standard deviation (SD) and compared using the independent Student's t-test. Categorical variables were expressed as frequencies and percentages (%) and compared using the Chi-square test or Fisher's exact test, as appropriate. A p-value of <0.05 was considered statistically significant.

Results

A total of 100 participants completed the study, with 50 in the IVF/ICSI group and 50 in the spontaneous conception (SC) group.

Baseline Characteristics: The baseline demographic and clinical characteristics of the two groups are presented in [Table 1]. The mean maternal age was significantly higher in the IVF/ICSI group compared to the SC group (32.4 ± 4.1 years vs. 28.1 ± 3.5 years, p < 0.001). There was no significant difference in Body Mass Index (BMI) or socioeconomic status between the groups. A higher proportion of women in the IVF/ICSI group were primigravida (84%) compared to the SC group (56%), a difference that was statistically significant (p = 0.002).

Table 1: Baseline Demographic and Clinical Characteristics of Study Participants

Characteristic	IVF/ICSI Group (n=50)	Spontaneous Conception Group (n=50)	p-value
Maternal Age (years)	32.4 ± 4.1	28.1 ± 3.5	<0.001
BMI (kg/m²)	24.8 ± 2.9	24.1 ± 3.2	0.235
Primigravida (%)	42 (84%)	28 (56%)	0.002
Socioeconomic Status			0.761
- Upper/Middle	38 (76%)	36 (72%)	
- Lower	12 (24%)	14 (28%)	

Data are presented as mean ± SD or n (%). p-values calculated using Student's t-test or Chi-square test.

Maternal Outcomes: The comparison of maternal outcomes is shown in Table 2. The incidence of GDM was significantly higher in the IVF/ICSI group (20%) than in the SC group (8%) (p = 0.041). Similarly, pre-eclampsia complicated a significantly greater proportion of pregnancies in the IVF/ICSI group (16% vs. 6%, p = 0.035). The rate of

Caesarean section was substantially higher in the IVF/ICSI group (62%) compared to the SC group (34%) (p = 0.003).

Table 2: Comparison of Maternal Outcomes

Maternal Outcome	IVF/ICSI Group (n=50)	Spontaneous Conception Group (n=50)	p-value
Gestational Diabetes Mellitus	10 (20%)	4 (8%)	0.041
Pre-eclampsia	8 (16%)	3 (6%)	0.035
Antepartum Haemorrhage	3 (6%)	1 (2%)	0.309
Mode of Delivery			
- Vaginal Delivery	19 (38%)	33 (66%)	0.003
- Caesarean Section	31 (62%)	17 (34%)	

Data are presented as n (%). p-values calculated using Chi-square test or Fisher's exact test.

Neonatal Outcomes: Neonatal outcomes are summarized in Table 3. The mean gestational age at birth was significantly lower in the IVF/ICSI group (38.2 ± 1.5 weeks) compared to the SC group (39.1 ± 1.1 weeks) (p < 0.001). Consequently, the rate of preterm birth (<37 weeks) was more than three times higher in the IVF/ICSI group (20% vs. 6%, p = 0.027). The mean birth weight of neonates was also significantly lower in the study group (2.9 ± 0.4 kg vs. 3.2 ± 0.3 kg, p < 0.001), with a corresponding higher incidence of low birth weight (<2.5 kg). The need for NICU admission was significantly higher for neonates born after IVF/ICSI (22%) compared to those spontaneously conceived (8%) (p = 0.031). There was no statistically significant difference in Apgar scores at 5 minutes.

Table 3: Comparison of Neonatal Outcomes

Neonatal Outcome	IVF/ICSI Group (n=50)	Spontaneous Conception Group (n=50)	p-value
Gestational Age at Birth (weeks)	38.2 ± 1.5	39.1 ± 1.1	<0.001
Preterm Birth (<37 weeks)	10 (20%)	3 (6%)	0.027
Birth Weight (kg)	2.9 ± 0.4	3.2 ± 0.3	<0.001
Low Birth Weight (<2.5 kg)	9 (18%)	3 (6%)	0.048
Apgar Score at 5 min < 7	3 (6%)	1 (2%)	0.309
NICU Admission	11 (22%)	4 (8%)	0.031

Data are presented as mean ± SD or n (%). p-values calculated using Student's t-test or Chi-square test.

Discussion

This prospective study provides valuable insights into the maternal and neonatal outcomes of IVF/ICSI pregnancies within the specific context of a North Indian tertiary care centre. Our findings demonstrate that pregnancies conceived via ART are associated with a significantly higher risk of adverse outcomes compared to spontaneously conceived pregnancies, even when restricted to singleton births.

A key finding of our study is the significantly higher mean maternal age in the IVF/ICSI group. This is a consistent observation across the literature, as advanced maternal age is a primary reason for seeking fertility treatment.[11] This age difference is a critical confounding factor that may independently contribute to the increased risk of complications such as GDM and pre-eclampsia.[12]

Our results showed a significantly higher incidence of GDM and pre-eclampsia in the IVF/ICSI group, which aligns with the findings of a large meta-analysis by Pandey et al.[13] The pathophysiology behind this increased risk is complex. It may be related to the hormonal milieu created during controlled ovarian stimulation, placental abnormalities stemming from the implantation of an in-vitro-cultured embryo, or the underlying subfertility factors themselves.[4,14]

The rate of Caesarean section was nearly double in the IVF/ICSI group in our cohort. This finding is ubiquitous in ART literature.[6] While some of this increase can be attributed to higher rates of medical indications like pre-eclampsia and fetal distress, a significant portion may be non-medically indicated. The perception of an ART pregnancy as a "precious" one by both clinicians and patients often lowers the threshold for operative delivery, a phenomenon that warrants further investigation and the development of clear guidelines to promote vaginal birth when safe.[15]

Regarding neonatal outcomes, our study confirmed that infants conceived via IVF/ICSI had a lower mean gestational age and birth weight, leading to higher rates of preterm birth and low birth weight. This is one of the most robustly documented risks associated with ART.[7,10] The increased risk of PTB and LBW persists even after controlling for maternal age and parity, suggesting that factors intrinsic to the ART process, such as the impact of embryo culture media or epigenetic modifications, may play a role.[16] These adverse neonatal outcomes directly explain the higher rate of NICU admissions observed in our study group, placing a greater burden on neonatal healthcare resources.

Limitations: This study has certain limitations. The sample size of 100 participants is relatively small, which may limit the statistical power to detect smaller differences in some outcomes. As a single-centre study, the findings may not be generalizable to the entire population. Although we excluded women with major pre-existing conditions, we could not control for all potential confounders, such as the specific cause of infertility or paternal factors, which may also influence pregnancy outcomes. Despite these limitations, the prospective nature of the study is a significant strength, allowing for accurate and uniform data collection and minimizing recall bias.

Conclusion

In conclusion, this prospective study from Kanpur confirms that

singleton pregnancies conceived through IVF/ICSI are associated with a significantly increased risk of adverse maternal outcomes, including gestational diabetes, pre-eclampsia, and Caesarean delivery, as well as adverse neonatal outcomes such as preterm birth, low birth weight, and NICU admission. The increased risk profile is likely a combination of the advanced maternal age and underlying subfertility of the patient population, as well as influences from the ART procedures. These findings emphasize that IVF/ICSI pregnancies should be managed as high-risk. They require meticulous antenatal surveillance, patient counseling regarding potential risks, and judicious decision-making regarding the mode of delivery to optimize outcomes for both mother and child. Further large-scale, multi-centre studies are needed to corroborate these findings and to help delineate the precise mechanisms responsible for these risks.

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Conflicts of interest
There are no conflicts of interest.

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