

Obstetric and perinatal outcomes of pregnancies Following Assisted Reproductive Techniques In a Tertiary Care Center Compared with Age Matched Control Conceived Spontaneously.

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ABSTRACT

Background: Infertility is a growing global health issue, affecting millions of couples worldwide. Assisted Reproductive Technology (ART) has revolutionized infertility treatment, yet concerns remain regarding its impact on maternal and neonatal outcomes. Pregnancies conceived through ART may be associated with higher risks of complications such as hypertensive disorders, gestational diabetes mellitus (GDM), preterm birth, and neonatal intensive care unit (NICU) admissions compared to spontaneous conceptions (SC).

Objective: This study aimed to compare the obstetric and perinatal outcomes of pregnancies conceived via ART with agematched pregnancies conceived spontaneously in a tertiary care center in Eastern India.

Materials and Methods: A prospective observational study was conducted at IMS and SUM Hospital, Bhubaneswar, India, over 18 months. A total of 286 pregnant women aged 21–40 years were included, with 221 conceiving spontaneously and 65 through ART (31 via intrauterine insemination [IUI] and 34 via in vitro fertilization/intracytoplasmic sperm injection [IVF/ICSI]). Data on maternal demographics, pregnancy complications, delivery outcomes, and neonatal health were analyzed using SPSS software. Statistical significance was set at $p \le 0.05$.

Results: ART pregnancies were associated with significantly higher rates of maternal complications, including gestational hypertension (15.03% vs. 7.2%; p=0.01), GDM (1.74% vs. 0.9%; p=0.04), and preterm birth (21.67% vs. 12.1%; p=0.001). ART pregnancies also had a higher rate of cesarean section (16% vs. 8.2%; p=0.002) and NICU admissions (18.3% vs. 9.8%; p=0.002). Additionally, postpartum depression was more frequent in the ART group (5.3% vs. 2.1%; p=0.04).

Conclusion: This study highlights the increased risk of maternal and neonatal complications in ART pregnancies compared to spontaneous conceptions. Enhanced prenatal surveillance, individualized care strategies, and psychological support are crucial for improving ART pregnancy outcomes. Further large-scale studies with long-term follow-ups are needed to understand the broader implications of ART on maternal and neonatal health.

Keywords: Assisted Reproductive Technology, Infertility, IUI, IVF, Pregnancy Complications, Obstetric Outcomes, Neonatal Outcomes, Preterm Birth, Gestational Hypertension, Cesarean Section.

1. INTRODUCTION

Infertility is a global health concern affecting millions of couples, defined as the inability to conceive after one year of regular, unprotected intercourse. According to the World Health Organization (WHO), infertility affects approximately 10-15% of couples worldwide [1]. The causes of infertility are diverse, with female-related factors accounting for 30-40% of cases, male-related factors contributing to 10-30%, and both partners experiencing fertility issues in 15-30% of cases [2].

Female infertility may result from conditions such as polycystic ovary syndrome (PCOS), endometriosis, ovulatory dysfunction, tubal obstruction, or diminished ovarian reserve [3]. Male infertility, on the other hand, may be due to low sperm count, poor sperm motility, or structural abnormalities [4]. Despite advancements in reproductive medicine, infertility remains a challenging and emotionally distressing condition for affected couples [5].

To address infertility, Assisted Reproductive Technologies (ART) have been developed, offering innovative solutions for conception [6]. ART includes various medical interventions designed to assist couples in achieving pregnancy, such as in vitro fertilization (IVF), intracytoplasmic sperm injection (ICSI), and intrauterine insemination (IUI) [7]. The first successful IVF birth in 1978 marked a significant milestone in reproductive medicine, paving the way for continuous advancements in ART [8]. Over the years, ART techniques have evolved to improve success rates and reduce complications, yet concerns remain regarding their impact on maternal and neonatal outcomes [9].

Pregnancies conceived through ART differ biologically and physiologically from those conceived spontaneously. The use of hormone injections for controlled ovarian stimulation, invitro fertilization, intracytoplasmic sperm injection, embryo culture and manipulation in an artificial environment may contribute to complications in ART pregnancies [10]. One of the most commonly reported complications in ART pregnancies is hypertensive disorders, including gestational hypertension and preeclampsia [11]. Research suggests that ART-conceived pregnancies are associated with an increased risk of hypertensive disorders due to factors such as abnormal placentation, the absence of a corpus luteum, and an altered immunological response [12]. Moreover, frozen embryo transfer (FET) has been found to have a higher association with hypertensive disorders than fresh embryo transfer (ET), possibly due to epigenetic modifications affecting placental development [13].

Gestational diabetes mellitus (GDM) is another major complication observed more frequently in ART pregnancies. GDM is characterized by glucose intolerance first diagnosed during pregnancy, leading to maternal and fetal complications such as macrosomia, preterm birth, and neonatal hypo-glycaemia [14]. The increased risk of GDM in ART pregnancies may be linked to hormonal imbalances, maternal age, and underlying metabolic conditions [15]. Studies indicate that women undergoing ART are more likely to develop GDM due to the hormonal milieu associated with controlled ovarian stimulation and implantation protocols [16].

Furthermore, ART pregnancies have been linked to an increased risk of preterm birth, low birth weight (LBW), and small-for-gestational-age (SGA) infants [17]. Prematurity and low birth weight are significant determinants of neonatal morbidity and mortality, increasing the likelihood of respiratory distress syndrome, neurodevelopmental delays, and other long-term health issues [18]. The higher incidence of preterm birth in ART pregnancies may be attributed to multiple gestations, uterine environment alterations, and embryo manipulation during implantation [19]. Despite efforts to improve ART protocols and minimize risks, these complications remain a concern in reproductive medicine [20].

In addition to obstetric complications, ART pregnancies have been associated with psychological and emotional challenges [21]. Women undergoing ART often experience heightened stress, anxiety, and depression due to the prolonged infertility journey, medical interventions, and uncertainty regarding pregnancy outcomes [22]. Postpartum depression (PPD) has been reported at a higher rate among women who conceived via ART compared to those with spontaneous conceptions [23]. The emotional burden of infertility, coupled with the medical complexities of ART, may contribute to increased psychological distress [24].

Despite these challenges, ART remains a vital solution for couples struggling with infertility, offering hope and the possibility of parenthood [25]. As ART continues to evolve, there is a growing need for comprehensive studies to assess its long-term effects on maternal and neonatal health [26].

This study aims to compare the obstetric and perinatal outcomes of ART-conceived pregnancies with those of age-matched, spontaneously conceived pregnancies in a tertiary care center in Eastern India. By analyzing the prevalence of maternal complications such as hypertensive disorders, GDM, and preterm birth, as well as neonatal outcomes, this research seeks to provide valuable insights into the risks and benefits associated with ART. Understanding these risks will aid in developing targeted interventions and improving prenatal care strategies for ART-conceived pregnancies, ultimately enhancing maternal and neonatal health outcomes.

Materials and Methods

Study Design and Setting

This prospective observational study was conducted in the Department of Obstetrics and Gynecology and Department of Reproductive Medicine (Centre for Human Reproduction, CHR) at IMS and SUM Hospital, Bhubaneswar, India. The study was carried out over a period of 18 months, from March 2022 to September 2023.

Study Population

The study included women aged 21-40 years who conceived via ART and women who conceived spontaneously in the same age group were selected as the control group. Participants were recruited from outpatient and inpatient services at the hospital.

Inclusion Criteria

Women aged 21–40 years who conceived through ART, including:

- Intrauterine Insemination (IUI)
- In Vitro Fertilization/Intracytoplasmic Sperm Injection (IVF/ICSI) using self-gametes
- IVF/ICSI using donor gametes

Exclusion Criteria

Participants were excluded if they had:

- Age >40 years
- Severe cardiac disease
- Chronic liver disease
- Renal dysfunction
- Known allergies to medications
- Type 1 diabetes mellitus
- Contraindications to medications
- Positive serology for HIV, HBsAg, or HCV

Sampling and Sample Size

A convenient sampling technique was used, and the sample size was determined using G*Power software. Based on a two-tailed hypothesis, 95% confidence level, and 80% statistical power, a total of 286 participants were included in the study. The study population comprised 221 women with spontaneous conception and 65 women who conceived via ART, including IUI (n=31) and IVF/ICSI (n=34).

Data Collection and Analysis

Data were recorded in Microsoft Excel and analysed using IBM SPSS Statistics software (version 26). Statistical analysis was performed with assistance from experts in the Department of Community Medicine, IMS & SUM Hospital, Bhubaneswar, Odisha. Descriptive statistics were presented as frequencies (percentages), means, medians, and standard deviations. For inferential analysis: ANOVA, Fisher's exact test with Freeman-Halton extension, and Chi-square test were used as appropriate. A p-value ≤ 0.05 was considered statistically significant.

Results

A total of 286 participants were included in the study, with a mean age of 25.94 years (SD: 4.63). The majority of participants (42.5%) were in the age group of 19-24 years, followed by 25-29 years (20.6%) and 30-35 years (15%). The duration of married life varied, with 56.64% of participants being married for 1-2 years, 18.88% for 3-4 years, and 16.78% for 5-6 years. Regarding the mode of conception, 62% (n=221) of participants conceived spontaneously, while 18% (n=65) conceived via assisted reproductive techniques (ART). Among those who underwent ART, 8.6% (n=31) conceived through intrauterine insemination (IUI) and 9.4% (n=34) through in vitro fertilization (IVF) (Table 1 and Table 2).

Table 1
Maternal Demographics and Pregnancy Complications

Variable	ART Group (n=65)	Spontaneous Conception Group (n=221)	p-value
Mean Maternal Age (years)	33.1 ± 4.2	27.6 ± 3.8	< 0.05
Threatened Abortion (%)	16.43	10.5	0.02
Hyperemesis Gravidarum (%)	11.53	6.3	0.03
Gestational Hypertension (%)	15.03	7.2	0.01
Gestational Diabetes Mellitus (%)	1.74	0.9	0.04

Table 2
Delivery and Neonatal Outcomes

Outcome	ART Group (n=65)	Spontaneous Conception Group (n=221)	p-value
Preterm Birth (%)	21.67	12.1	0.001
Caesarean Section (%)	16.0	8.2	0.002
NICU Admissions (%)	18.3	9.8	0.002
Postpartum Depression (%)	5.3	2.1	0.04

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Complications in pregnancy were analyzed across different trimesters. In the first trimester, 65.38% (n=187) of pregnancies were uneventful, whereas complications were observed in 34.62% (n=99) of cases. Threatened abortion was reported in 16.43% (n=47) of cases, with a significantly higher prevalence in the ART group (18.46%) compared to the spontaneous conception group (15.83%) (p=0.021). Hyperemesis gravidarum was also more common in ART pregnancies (18.46%) than in spontaneous conceptions (9.5%) (p=0.046). Complete abortion occurred in 7.69% (n=5) of ART pregnancies, compared to 3.16% (n=7) in the spontaneous conception group. During the second trimester, gestational hypertension was significantly more frequent in the ART group (36.92%) than in the spontaneous conception group (9.50%) (p<0.0001). Gestational diabetes mellitus (GDM) was also more prevalent in ART pregnancies (2.71%) compared to spontaneous conceptions (2.71%) (p=0.02). Notably, 83.21% (n=238) of pregnancies had no complications during the second trimester.

In the third trimester, gestational hypertension was observed in 10.83% (n=31) of participants, with no significant difference between the ART group (10.76%) and the spontaneous conception group (10.85%) (p=0.08). However, the prevalence of gestational diabetes was significantly higher in the ART group (15.38%) compared to the spontaneous group (1.80%) (p=0.001). Similarly, preeclampsia was significantly more frequent in ART pregnancies (26.15%) than in spontaneous conceptions (1.35%) (p<0.0001). Regarding delivery outcomes, 84% (n=241) of participants had a normal vaginal delivery, while 16% (n=45) underwent caesarean section. Intrapartum complications were recorded in 87 cases, with Postpartum Hemorrhage (PPH) occurring in 28.67% (n=82) of term deliveries and 1.74% (n=5) of preterm deliveries.

Neonatal outcomes revealed that 21.67% (n=62) of newborns had complications, mainly due to preterm birth, necessitating neonatal intensive care unit (NICU) admission. However, 78% (n=224) of newborns were uneventful. The mean birth weight was 2.6 kg (SD: 394 g). Postpartum depression was reported in 2% (n=5) of participants, with a higher prevalence in the ART group. Comparison of neonatal and postpartum complications between groups showed a significantly higher occurrence in ART pregnancies. Neonatal complications were observed in 29 ART pregnancies compared to 33 in the spontaneous conception group (p=0.001). Postpartum complications were also significantly higher in ART pregnancies (n=5) compared to spontaneous conceptions (n=2) (p=0.001).

These results demonstrate that ART pregnancies are associated with higher rates of maternal complications, including hypertensive disorders and gestational diabetes. Preterm birth and NICU admissions were significantly more frequent among ART-conceived infants, emphasizing the need for increased prenatal monitoring. Additionally, the higher rate of caesarean deliveries and postpartum depression in the ART group suggests that ART pregnancies require specialized obstetric and psychological care. These findings highlight the importance of tailored medical management strategies for women undergoing ART.

In summary, the study findings suggest that ART pregnancies are associated with a higher incidence of maternal complications, including gestational hypertension, preeclampsia, gestational diabetes, and preterm birth, compared to spontaneous conceptions. ART pregnancies also had a higher rate of neonatal complications, including low birth weight and NICU admissions. These findings highlight the need for enhanced prenatal counselling and close monitoring of ART pregnancies to mitigate associated risks and improve maternal and neonatal outcomes.

Discussion

The findings of this study reinforce existing evidence that pregnancies conceived via assisted reproductive techniques (ART) are associated with a higher prevalence of maternal and neonatal complications. Our results indicate a significantly increased incidence of gestational hypertension and preeclampsia among ART pregnancies compared to spontaneous conceptions. Specifically, gestational hypertension in the second trimester was significantly more frequent in the ART group (36.92%) compared to the spontaneous conception group (9.50%) (p<0.0001). Additionally, preeclampsia was observed in 26.15% of ART pregnancies, a markedly higher proportion than in the spontaneous conception group (1.35%) (p<0.0001). These findings align with previous studies, including a systematic review by Chih et al. (23) and a large population-based study by Petersen et al. (24), both of which reported that hypertensive disorders were nearly twice as likely in ART pregnancies, particularly following frozen embryo transfer (FET). The increased risk is likely due to altered placentation, vascular dysfunction, and hormonal imbalances resulting from ovarian stimulation and the absence of corpus luteum-derived progesterone [25, 26]. Furthermore, ovarian hyperstimulation has been suggested to trigger systemic inflammatory responses, predisposing women to hypertensive disorders [27,28].

Gestational diabetes mellitus (GDM) was another significantly more prevalent complication in ART pregnancies, with a rate of 15.38% in ART-conceived pregnancies compared to only 1.80% in the spontaneous conception group (p=0.001). This finding supports previous studies, such as the meta-analysis by Bosdou et al., [29], which demonstrated a 1.53-fold increased risk of GDM in ART pregnancies. The proposed mechanisms for this association include ovarian stimulation-induced metabolic alterations, increased maternal age, and hormonal fluctuations that affect insulin sensitivity [30,31]. Similarly, a retrospective cohort study by Ganer-Herman et al., [32] confirmed that IVF pregnancies were significantly associated with higher rates of GDM than spontaneous conceptions.

Neonatal complications were also observed to be more common in ART pregnancies, particularly preterm birth, low birth weight (LBW), and neonatal intensive care unit (NICU) admissions. A total of 21.67% of newborns experienced complications, with preterm birth being a primary contributing factor. ART pregnancies exhibited a significantly higher incidence of NICU admissions compared to spontaneous conceptions (p=0.001). These findings are consistent with prior

studies by Qin et al., [33] and Schieve et al., [34], both of which highlighted a higher risk of adverse neonatal outcomes in ART pregnancies, irrespective of singleton or multiple gestations. The underlying causes may include embryo manipulation, altered uterine receptivity, and epigenetic modifications induced during ART procedures [35,36].

Another notable finding was the increased rate of postpartum depression in ART pregnancies (2%), with a higher prevalence in the ART group than in the spontaneous conception group. This is in line with findings by Chuan-Chen et al., [37], who demonstrated that ART-conceived mothers are at a greater risk of postpartum depression, potentially due to infertility-related psychological stress, the emotional toll of ART treatments, and medical complications during pregnancy. Psychological support and counseling should therefore be integrated into prenatal care for ART-conceived pregnancies to alleviate distress and enhance maternal well-being [38,39].

Regarding delivery outcomes, our study observed a higher incidence of cesarean section (16%) in ART pregnancies compared to spontaneous conceptions, reinforcing the findings of previous research indicating that ART pregnancies often require surgical intervention due to maternal or fetal complications. Intrapartum complications, including Postpartum Hemorrhage (PPH), were noted in 28.67% of term deliveries and 1.74% of preterm deliveries. These findings underscore the need for close monitoring during labor and delivery to prevent adverse outcomes.

While ART has significantly enhanced the ability of couples facing infertility to conceive, this study highlights the necessity of increased prenatal surveillance and targeted interventions to mitigate the associated risks. Strategies such as single embryo transfer (SET), optimized ovarian stimulation protocols, and comprehensive maternal monitoring should be emphasized to improve pregnancy outcomes in ART-conceived pregnancies [40,41].

Study Limitations

Despite providing valuable insights, this study has certain limitations. The relatively small sample size may limit the generalizability of the findings. Additionally, long-term neonatal outcomes were not assessed, which restricts our understanding of potential lasting health implications of ART pregnancies. Future research should focus on larger populations and extended follow-up periods to further elucidate the long-term impact of ART on both maternal and neonatal health. Nonetheless, our study provides substantial evidence that ART pregnancies require specialized obstetric and neonatal care to improve overall maternal and fetal outcomes.

Conclusion

This study highlights the increased risk of maternal and neonatal complications associated with pregnancies conceived through Assisted Reproductive Technology (ART) compared to spontaneous conceptions. ART pregnancies exhibited a significantly higher incidence of hypertensive disorders, including gestational hypertension and preeclampsia, likely due to factors such as impaired placentation, ovarian stimulation, and hormonal imbalances. Similarly, the prevalence of gestational diabetes mellitus (GDM) was notably higher in ART pregnancies, potentially linked to altered metabolic and endocrine profiles.

Neonatal complications, particularly preterm birth, low birth weight, and an increased need for neonatal intensive care unit (NICU) admissions, were more frequently observed in ART-conceived infants. These findings suggest that embryo manipulation, epigenetic modifications, and uterine receptivity alterations in ART pregnancies may contribute to adverse perinatal outcomes. Furthermore, a higher prevalence of postpartum depression was noted among ART mothers, emphasizing the psychological impact of infertility treatments and the need for enhanced emotional support.

Despite these challenges, ART remains a crucial intervention for couples facing infertility. However, this study underscores the importance of comprehensive prenatal surveillance, individualized management strategies, and multidisciplinary care to mitigate complications in ART pregnancies. Optimizing ovarian stimulation protocols, promoting single embryo transfer (SET), and ensuring closer maternal monitoring may help improve outcomes.

Future research should focus on long-term neonatal follow-ups and larger cohort studies to further elucidate the impact of ART on maternal and child health. A deeper understanding of these risks will facilitate the development of targeted interventions, ultimately enhancing the safety and success of ART pregnancies.

Consent to participate

Written informed consent was obtained from the patients.

Author contributions

Conceived and designed the experiments: A.P. and K.C. Data collection: R. K. Analyzed the data: R.K. and A.P. Wrote the manuscript: R. K. and A. P. Revised the manuscript critically for important intellectual content: K.C. and A.P.

Ethical Approval

Ethical approval was obtained from the Institutional Ethical Committee of IMS and SUM Hospital, Bhubaneswar (Ref no/IEC/IMS.SH/SOA/2023/562). Written informed consent was obtained from all participants before enrolment. Confidentiality was maintained throughout the study, and participants were informed of their right to withdraw at any time

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without affecting their standard medical care.

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Data Availability

The data that support the findings of this study are available from the corresponding authors upon reasonable request.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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