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**Original Research Article**

# Assessment of maternal factors and fetomaternal outcome in pregnant women conceived by artificial reproductive techniques

**Deepika Jatav*, Nootan Chandwaskar, Madhuri Arya**

Department of Obstetrics and Gynecology, Sri Aurobindo Medical College and PG Institute Indore, Madhya Pradesh, India

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***Correspondence:**
Dr. Deepika Jatav,
E-mail: deepika03jatav@gmail.com



## ABSTRACT

**Background:** Infertility is a major issue and a source of social and psychological suffering for many couples. Introduction of assisted reproductive technology (ART) leads to great relief for couples nowadays.
**Methods:** This present observational cross-sectional study was conducted at OBGY Department at Sri Aurobindo Medical College and Post Graduate Institute, Indore and who satisfy the inclusion criteria was studied from 1st April 2021 to 30th September 2022 (18 months). After approval from Institutional ethical committee. Each patient fulfilling the inclusion criteria was included in the study. Informed written consent was taken.
**Results:** The mean age of women in this study was 37.6 years and the most common age group was between 30-50 years. Infertility was mostly unexplained (40%), followed by female factor (33.33%), male factor (16.67%), and combined (10%). 63.33% were singletons, 36.67% twins. Preterm labor (43.33%) was most common. Preeclampsia/eclampsia (33.33%), gestational hypertension, renal failure, gestational diabetes, cardiomyopathy, hepatic failure, HELLP syndrome, and DIC were other complications. 60% were caesarean-sectioned and 40% vaginal delivery. 90.24% of neonates had 5-minute Apgar scores above 7 and 9.76% below 7. 4 stillbirths (9.76%) and 75.68% of live births required NICU admission. 5 neonatal deaths (12.2%) and 21.95% perinatal mortality.
**Conclusions:** There are numerous maternal and perinatal complications linked to ART. Couples should therefore be counselled about these risks while offering them ART as a mode of conception.

**Keywords:** ART, Adverse outcomes of ART, Infertility, Perinatal complications, Renal failure

## INTRODUCTION

An increasing number of babies are born worldwide as a result of ART procedures due to developing technologies and the number of fertility clinics offering assisted reproductive technology (ART).[1,2] ART pregnancies make up 1.5 to 5.9% of all births in high-income countries.[3-6] Despite ART's success in treating infertility, worries about its safety and impact on maternal and child health are growing. Previous research found that, even when limited to singleton births, pregnancies after ART are associated with a higher risk of adverse neonatal outcomes, such as preterm delivery, low birth weight, birth defects, and perinatal mortality.[6-10] The use of intracytoplasmic sperm injection (ICSI) and/or in vitro fertilisation (IVF) as part of ART has been linked to a higher risk of unfavourable perinatal outcomes, according to data from two meta-analyses.[7,11] Increased risk for maternal health has also been suggested by some studies, including those on hypertensive complications related to pregnancy, gestational diabetes, and other maternal morbidity.[7,12,13] However, according to some studies, those unfavourable health-related outcomes are not attributable to the ART procedures connected to IVF and ICSI. Studies of sub fertile women who gave birth naturally without the use of ART and still showed an increased risk of poor maternal and neonatal outcomes support this hypotheses.[14,15] To address this issue, numerous studies have been carried out,

but the outcomes are frequently unreliable. The use of medications, an altered hormonal environment at the time of implantation, manipulation of gametes and embryos, or a combination of these, have all been suggested as potential causes of the poorer perinatal health of ART-mothers and children.[8,16,17] Additionally, it has been discovered that, when compared to a natural pregnancy, the risk for preterm birth rises with ART low-technology treatments and rises even more with ART high-technology treatments.[18] The results that are currently available are debatable and there is little information available about how the type of ART used affects maternal and live-birth outcomes. Additionally, it has been asserted, that the poorer health of infants is primarily caused by the higher risk incidence of multiple pregnancies and is unrelated to ART procedures.[19,20]

Multiple gestations, preterm deliveries, gestational diabetes mellitus, pregnancy-induced hypertension, preeclampsia, and placenta previa are among the maternal complications associated with ART pregnancy that are more common. There is also a higher likelihood of surgical intervention in ART pregnancies.[21] The most notable factor linked to a poor pregnancy outcome in ART is multiple pregnancy.[22-25] Additional risks associated with ART pregnancies include chromosomal abnormalities in foetuses, stillbirths, low birth weight, preterm birth, adverse neurodevelopmental outcomes, and high infant mortality.[22-24] India is currently emerging as a major ART hub worldwide. The price of ART in India ranges from Rs. 1 to 1.5 lakhs per cycle. Since India's economy has grown, many infertile couples can now afford this cutting-edge ART procedure. Unfortunately, there is a strong correlation between complications during pregnancy and delivery and assisted conception. Couples seek treatment at tertiary care facilities for these complications when their resources are already exhausted. In cases referred to our tertiary care hospital, the goal of this study is to ascertain the maternal and foetal outcome following assisted reproductive technology.

To better understand the impact of ART on maternal and child health, this study trying to Assess maternal factors and fetomaternal outcome in pregnant women conceived by artificial reproductive techniques.

## METHODS

This present Observational cross-sectional study was conducted at Obstetrics and Gyneacology Department at Sri Aurobindo Medical College and Post Graduate Institute, Indore and who satisfy the inclusion criteria was be studied from 1st April 2021 to 30th September 2022 (18 months). After approval from Institutional ethical committee. Each patient fulfilling the inclusion criteria was be included in the study. Informed written consent was taken. The study population was selected from patients admitted to labour room for delivery/conservative management, conceived by artificial reproductive techniques in SAMC&PG Institute& BHRC hospital after applying inclusion and exclusion criteria. A pre-structured proforma was used to collect the baseline data. Detailed clinical examination and biochemical tests was done on all patients as per the protocol.

Inclusion Criteria- Pregnancy convinced by Artificial Reproductive techniques with any presentation. Pregnancy convinced by other than artificial reproductive techniques/spontaneously were excluded. Patients attending OPD/ IPD of SAIMS and PG Institute fulfilling the inclusion criteria was be included in the study. Detailed history, clinical examination and lab investigations of the patient was done. All the patient fulfilling the inclusion criteria was be thoroughly investigated. All the relevant menstrual, obstetric, medical, personal and surgical history along with thorough clinical examination was done. Descriptive statistic was used to show features and characteristics of the data. Chi square test was used to show association. P value less than 0.05 was considered as statistically significant.

## RESULTS

Th Based on the inclusion and exclusion criteria, a total of 60 cases were included in the current study. Out of 60, 51 cases were referred to our hospital for treatment of pregnancy-induced complications following ART conception, and 9 cases were subsequently registered at our hospital for routine pregnancy management. The sociodemographic details of the women who participated in the current study were noted. The age distribution of the cases is shown in Table 1 below, where it can be seen that four women (6.67%) were the older than 50 years old and that 60% of the women were in the 30–50-year age range.

**Table 1: Age distribution of the women conceived through ART.**

| Age in years | Number of cases (n=60) | % |
|---|---|---|
| **<30** | 20 | 33.33 |
| **31-40** | 18 | 30 |
| **41-50** | 18 | 30 |
| **>50** | 4 | 6.67 |

**Table 2: Years of married life of ART conceived women.**

| Years of married life | Number of cases (n=60) | % |
|---|---|---|
| **< 5** | 20 | 33.33 |
| **5-10** | 26 | 43.33 |
| **11-15** | 10 | 16.67 |
| **16-20** | 2 | 3.33 |
| **>20** | 2 | 3.33 |

The women who were a part of this study had chosen ART for conception after having been married for a variety of lengths of time. One third of women (33.33%) and the majority (43.33%) of women had been married for less

than five years respectively. Out of the remaining, 16.67% had been married for between 11 and 15 years, 3.33% for between 16 and 20 years, and 9.33% had been married for more than 20 years. Table 2 below provides examples of the above-mentioned information.

**Table 3: The various causes of infertility.**

| Cause of infertility | Number of cases (n=60) | % |
|---|---|---|
| **Male factor** | 10 | 16.67 |
| **Female factor** | 20 | 33.33 |
| **Both male and female factor (combined factor)** | 6 | 10 |
| **Unexplained** | 24 | 40 |

**Table 4: Types of gestation.**

| Gestation type | Number of cases (n=60) | % |
|---|---|---|
| **Singleton pregnancy** | 38 | 63.33 |
| **Multiple pregnancy (twin pregnancy)** | 22 | 36.67 |

Male factor, female factor, unexplained, and male and female factor combined were studied as the main causes of infertility. Male factor infertility was found in 16.67% of cases, female factor infertility in 33.33%, and both male and female factor infertility were found in 10% of cases. In 40% of cases, the cause was left unidentified.

The most frequent cause of infertility in the current study, closely followed by female factor infertility. Additionally, primary infertility affected 50% of the cases. The following table (Table 3) provides a list of the primary causes of infertility in the current study.

***Type of gestation***

In the current study, it was found that 63.33% of pregnancies were singletons and 36.67% were twin pregnancies. In the current study, there were no higher order pregnancies. The different gestational type is listed in (Table 4) below.

***Pregnancy and perinatal complications***

Pregnancies resulting from ART had a sizable number of pregnancy complications. Additionally, compared to natural conception, perinatal complications were more frequently observed in ART conception. Only 14 (23%) out of the 60 patients who were enrolled in the current study did not have any complications during pregnancy or the perinatal period, leaving 46 (77%) patients with pregnancy related complications. Some patients experienced more than one complication; as a result, there were more complications overall than there were patients.

For the management of pregnancy-related complications, a total of 18 out of 46 patients (or 30% of the total 60 patients) required admission to an intensive care unit. In the current study, there were no maternal mortalities. Due to the need for labour induction in these patients due to maternal complications, the preterm delivery rate was higher in the current study.

**Table 5: Pregnancy related complications seen in ART pregnancies.**

| Complication observed | Number of patients with the complication | % |
|---|---|---|
| **Gestational hypertension** | 14 | 23.33 |
| **Preeclampsia /eclampsia** | 20 | 33.33 |
| **Renal failure** | 10 | 16.67 |
| **Hepatic failure** | 4 | 6.67 |
| **Disseminated intravascular coagulation** | 4 | 6.67 |
| **Gestational diabetes** | 8 | 13.33 |
| **Intracranial bleed** | 2 | 3.33 |
| **Cardiomyopathy** | 8 | 13.33 |
| **Pancreatitis** | 2 | 3.33 |
| **HELLP syndrome** | 4 | 6.67 |
| **Preterm labour** | 26 | 43.33 |

26 patients out of 60 had preterm deliveries, including 18 twin pregnancies and 8 singleton pregnancies. The following is a list of the pregnancy related complications that were observed in this study (Table 5).

***Mode of delivery***

In pregnancies after assisted reproductive technology, surgical deliveries were more frequent. The most frequent delivery method was a caesarean section, which is indicative of the high incidence of maternal and foetal complications in the population under study. 24 women gave birth vaginally, out of whom 2 required an outlet forecepe, while 18 (50%) required a caesarean section for fetal distress. Followed by malpresentation in 10 patients (28%). The other finding included placenta previa in 2 patients (5%), non-progress of labour in 6 patients (17%), and others.

***Perinatal result***

Out of a total of 60 cases, 22 women had twin pregnancies and 38 women had singleton pregnancies. Following ART conception, the perinatal outcome of 82 babies in total was studied. In the current study, the perinatal outcome was examined in terms of Apgar scores at 5 minutes, the number of neonates who needed admission to a neonatal intensive care unit, the number of stillbirths, and the number of neonatal deaths. 90.24% of new-borns had an

Apgar score of 7 or higher, while 9.76% of new-borns had an Apgar score of less than 7, as shown in (Table 6).

**Table 6: Apgar score at 5 minutes after birth.**

| 5-minute Apgar score | Number of neonates (n=82) | % |
|---|---|---|
| <7 | 8 | 9.76 |
| ≥ 7 | 74 | 90.24 |

Due to pregnancy-related complications, all 8 of the stillborn babies were extremely premature, with gestational ages around 24–25 weeks. Induction of labour was performed on them for the benefit of the mother. NICU care was required for 56 infants out of 74 live births (75.68%), primarily because of preterm birth and low birth weight. Out of 56 NICU admissions, 44 babies required NICU care because they were premature, six babies had intrauterine growth retardation, and six babies had both prematurity and IUGR. 46 out of 56 infants, or (82.14%), had favourable NICU outcomes and were discharged alive. Ten infants died during the neonatal period, for a total neonatal death rate of 10.2%. Extreme prematurity with birth weight less than 700 grammes was the cause of 6 neonatal deaths.

**Table 7: NICU outcome of babies admitted to NICU.**

| NICU outcome | Number of babies (n=56) | % |
|---|---|---|
| **Neonatal death** | 10 | 17.86 |
| **Discharged alive** | 46 | 82.14 |

Table 7 provides an explanation of NICU outcomes. Out of 82 births, there were 18 perinatal deaths in total (stillbirths and neonatal deaths included). Thus, 21.95% of perinatal deaths were overall.

## DISCUSSION

Due to rising infertility rates, ART is a life science on the rise. Infertility rates are rising due to a faster pace of life, increased work pressure, worsening environmental pollution, and delayed marriage, elder age at first conception.

Women in this study averaged 37.6 years old. Over half of the women were 30-50 years old (60%), one third were under 30 (33.33%), and only 2 were over 50 (6.67%). Our findings were similar to a Republic of China study by Jie Z et al., where the mean age of ART-conceived women was 32.53.7. Pregnancies In this study, 36.3% had twins and 63.3% singletons. In a Zhejiang University study by Jie Z et al., 62.8% of ART conceptions were singletons and 37.2% were twins.[26] In vitro fertilisation now uses single embryo transfer, which explains this. Avoiding multiple pregnancy complications is the main reason. Obstetrical issues ART pregnancies had many complications. Preterm labour was the most common complication in our study (43.33%). Preeclampsia/eclampsia (33.33%) and gestational hypertension (23.33%) were the next most common complications. Renal failure (16.67%), gestational diabetes (13.33%), cardiomyopathy (13.33%), hepatic failure (6.67%), HELLP syndrome (6.67%), DIC (6.67%), and rare complications like intracranial bleed and pancreatitis (3.33%). Gao et al. found that ART conception was associated with preterm delivery, low birth weight, and small for gestational age babies.[27] IVF/ICSI pregnancies had a higher preterm delivery rate, as did Zhang et al ART.'s group, which also had higher rates of pre-eclampsia and gestational diabetes mellitus.[28] Preeclampsia/eclampsia, gestational diabetes, intrahepatic cholestasis, placenta previa, placental abruption, polyhydramnios, and postpartum haemorrhage were also reported in ART conceptions by Zhu et al.[26] Wang AY et al. found 82% caesarean section rates in ART patients in Australia.[29] This study showed comparable but slightly lower rates. 60% of our patients had caesarean sections, 40% vaginal delivery. The pregnancy is precious after long periods of infertility, so fewer patients try vaginal delivery and most opt for elective caesarean sections. Multiple pregnancies are more common in ART pregnancies and are associated with poor perinatal outcomes. Thus, many countries use elective single embryo transfer (e SET) and additional cycles with frozen/thawed embryos to reduce multiple pregnancies.[30]

Current evidence suggests that even singleton ART pregnancies are riskier. ART increases adverse outcomes for unknown multifactorial reasons. ART-treated women's underlying infertility diagnoses may cause adverse outcomes. ART, including embryo culture and cryopreservation, may harm ART offspring. Ovarian hyperstimulation also affects perinatal outcomes.[27] This study examined Apgar scores at 5 minutes, neonatal intensive care unit admissions, stillbirths, and neonatal deaths. Resuscitation response can be assessed by the 5-minute Apgar score and its change between 1 and 5 minutes. The neonatal resuscitation programme recommends repeating Apgar scores every 5 minutes for up to 20 minutes if they are less than 7. 12 90.24% of neonates had an Apgar score of 7 or higher at 5 minutes, indicating that peripartum hypoxia or ischemia did not cause neonatal encephalopathy. 9.76% had a score of less than 7. ART babies had a higher rate of low 5th-minute Apgar scores (<7) than spontaneous babies, according to Daniel Y et al.[31] Pourali L et al. found no significant increase in low 5-minute Apgar scores between ART and spontaneous conception. Their small sample size and lower preterm birth rate may explain this.[32] In this study, 75.68% of babies needed NICU care due to preterm birth and low birth weight. Caserta et al. and Daniel Yet al. found high NICU rates.[31,33] Wang et al. found 66% neonatal admission to intensive care units in ART pregnancies in Australia.[29] 4 still births and 5 neonatal deaths resulted in a 21.95% perinatal death rate. Chughtai AA et al. found a 16.5% perinatal death rate.[34]

## CONCLUSION

Thus, a range of maternal and perinatal complications are linked to assisted reproductive technology. The older age of the women who choose it, the history of infertility in these couples, and the high-risk factors connected to it could be some of the main causes of this. In order to reduce these risks, couples should be given advice while receiving ART as a method of conception. ART should only be used as a last resort in couples who have tried and failed with all other infertility treatment options, despite the fact that it is a very promising and useful mode of conception.

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