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## Assisted Reproductive Technology And Its Associated Adverse Outcomes On Mothers

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### ABSTRACT

Assisted reproductive therapy (ART) is available for infertile couples. Although it has a success rate but more complications to the risk of both mother and fetus. Proper protocol standardization and training programs are needed to overcome adverse outcomes. This article aims to assess the association of ART and its adverse outcomes on mothers. A review was performed for relevant literatures in the MEDLINE/PubMed, and Cochrane databases. We selected the literature that completed the inclusion criteria of the study. It is concluded that ART is associated with increased multiple pregnancies, hypertensive disorders, preterm birth, increase chances of cesarean section, stress and anxiety in couples and financial burden with an increasing dropout rate

**Keywords:** - Assisted reproductive therapy, hypertensive disease, Diabetes Mellitus, invitro fertilization, Intracytoplasmic sperm injection.

### INTRODUCTION

Infertility is the inability to conceive a pregnancy despite of unprotected sexual intercourse after one year of marriage. Infertility is a global problem, in the United State among heterosexual women aged fifteen to forty-nine years, about 19% of women are infertile and 26% have difficulty getting pregnant and among Indian women rate of infertility vary widely from state to states such as 3.7 in Utter Pradesh, Himachal Pradesh and Mumbai, to five percent in Andra Pradesh and fifteen percent in Kashmir (Adamson et al., 2011). Infertility is not always in women but men's problems too (CDC). According to CDC in this technological era, individuals who are not able to conceive can use assisted reproductive therapy (ART), a beautiful example is United state where about 1.9% of child were born through ART (Amanda kallen, 2021).The overall prevalence of infertility is associated wthe ith age of marriage (8.9%), nuclear family, employed mother, high contraceptive use, tobacco and alcohol consumption, PCOD, family history of infertility, obesity, irregular mensuration, and psychological factors such as depression and stress (Katole & Saoji, 2019; Zakerihamidi M et

al., 2015).

Like other countries, India has many ART centres in capital cities and a number of ART cycles are performed every year. Only they need to standardization of proper protocol, reporting and document the tremendous work being done has to maintain (Malhotra et al., 2013).

Use of ART has increased dramatically worldwide and helps to fulfil the wish of infertile parents but IVF is expensive with risk factors for maternal as well as fetus such as the increased risk for ovarian cancer, bleeding, infection, damage to bowel and bladder, multiple pregnancies, preterm delivery, very low birth weight baby, handicapped baby.

The risk of miscarriage is 15% to 50% for women in their ages 20s to 40s respectively. Risk of ectopic pregnancy 1% after IVF with lower back pain, low blood pressure, fainting, and sharp pain ("Perinatal Risks Associated With Assisted Reproductive Technology," 2016) .

Female infertility is associated with abnormal body mass index an imbalance in leptin and estrogen hormone (Imterat et al., 2019). The development of congenital heart disease, preterm baby, low birth weight, neurological problems, increase blood pressure in children and other perinatal outcomes were significantly increased in IVF conception as compared to non-IVF conception (Allen et al., 2006; Dunietz et al., 2015; Giorgione et al., 2018a; MCEL RATH, 1997; Okun et al., 2014). Obstetric outcomes related to fresh blastocyst transfer are showed a higher risk of placenta related diseases in which placenta previa and hypertensive disorders of pregnancy are the most common pregnancy complications and cause maternal death (Chih et al., 2021; da Silva et al., 2020; Nagata et al., 2019). The hypertensive diseases are associated with advanced age, diabetes Mellitus, and several comorbidities involved. Mothers with ART treatment showed a more risk of abruption placenta, placenta previa, morbid adherent placenta, blood transfusion and need for intensive care than non- ART mothers (Kathpalia et al., 2016)

Still today because of infertility, our Indian women were facing discrimination, social exclusion, and abandonment ultimately leads to mental health distress (Katole & Saoji, 2019). Perinatal outcomes from ART tend to affect every system of the body as the increased risk of major non-chromosomal birth defect (18%), blastogenesis defect, cardiovascular defect, musculoskeletal defect and genitourinary defect (Luke et al., 2021). The adverse outcomes can be reduced by proper handling of gamete during each procedure such as oocyte retrieval, insemination, embryo culture and embryo transfer in IVF (Sullivan-Pyke et al., 2017).

## **METHODOLOGY**

More than half of the studies were taken from PubMed and MEDLINE and a few from Cochrane journals.

S.k. Kathpalia et al. (2016) conducted a prospective study on complications in pregnancies after IVF and embryo transfer in India. The objectives of the study were to find out the complications and mode of delivery. After a detailed history, clinical examination and necessary investigation, a total of 130 cases were included and followed throughout pregnancy and labour. Study found 6 cases of missed abortion (4.6%), 4 cases of ectopic pregnancy (3%), threatened abortion (19.2%), gestational diabetes (6.1%), PIH (8.5%), preeclampsia (4.6%). The study concluded that among these women most commonly

primary infertility and multiple pregnancies were common.

Nagata C et al. conducted a cohort study in Japan on, negative health problems in the perinatal period among those who had taken ART therapy. The objective of the study was to differentiate problems associated with ART on mother and baby from those conceived naturally. The results showed that the women conceived with IVF-ET had a greater risk of placental-related problems and cardiac problems such as placenta previa and PIH at (adjusted OR 2.90 [95% CI 1.94, 4.34]) and (1.40 [1.10, 1.78]), respectively. On the other hand, abruption placenta is more common in women with ICSI (2.16 [1.20, 3.88]) as well as placenta previa (2.01 [1.29, 3.13]). The study concluded that both mother and child had a high risk of complications one should aware of the adverse outcome of ART.

Silva SG et al. (2020) conducted a cohort study on perinatal outcomes in pregnancies following assisted reproductive technology. The objective was to differentiate perinatal problems after ART from spontaneous conception. The study showed that the babies (n=23) born by ART had a lower mean of age and lower anthropometric assessment at birth  $p < 0.001$  when compared to spontaneous pregnancy (n=4252). The study concluded that the difference in child outcomes was because of multiple pregnancies and further research is needed to find out adverse outcomes from ART singleton pregnancies.

Hui Ju Jin et al. (2021) conducted a meta-analysis on reproductive and hypertensive disorders in pregnancy. After covering 1879 articles and 283 full-text articles, they included 85 articles of EMBASE, MEDLINE and Cochrane Library. The study was conducted to find out the comparison between hypertensive disorder during pregnancy and preeclampsia between IVF/ICSI pregnancies and spontaneous pregnancies. The study showed that pregnancy with IVF/ICSI had a higher number of HDP and preeclampsia than spontaneous pregnancies, especially in frozen embryo transfer.

Jiabi Qin et al. (2017) conducted a prospective cohort study for three years in China. the objectives of the study were to differentiate pregnancy-related problems in subfertile women from IVF treatment in women with a natural pregnancy. The mothers were divided into three groups, the IVF group (1260), the sub-fertile group (1899) and the fertile group (2480). Results showed that adverse obstetric outcomes were more associated with IVF and sub-fertile groups compared to the fertile group. The study found that among the groups the IVF group had a higher risk of GDM, PROM, LBW, perinatal mortality and congenital malformation.

Banker M et al. (2016) conducted a prospective follow-up study on pregnancy outcomes and complications of pregnancies after in-vitro fertilization. The objective of the study was to assess the prevalence of mother and child outcomes and adverse problems following embryo transfer in IVF/ICSI. Mothers were divided into three categories, category A (fresh embryo transfer using self oocyte: 691), category B (fresh embryo transfer using donor oocytes:810) and category C (thaw embryo transfer using vitrified warmed embryos:611), respectively. The results showed that the incidence rate of ectopic pregnancy was more in group A (2.8%) as compared to group B (1.6%) and GROUP C (1.1%), multiple pregnancy rate was higher in

group B (32.5%) compared to group A (27.3%) and group C (31.3%), and maternal complications were more in group B (23.7%) than group (17.7%) and group C (17.8%). They concluded that a higher incidence of complications on in oocyte donors may be because of advanced maternal age, different placentation and low immunity.

Pinborg A et al. (2013) conducted a systemic review on why singleton conceived after assisted reproduction technology has adverse perinatal outcomes. The authors searched data from 1982 to 2012 by using PubMed and Cochrane databases. Out of 1255 articles, 65 articles met their inclusive criteria They excluded studies using donor or frozen oocytes. The study found that subfertility leads to adverse perinatal outcomes whereas hormonal stimulation and IVF methods play a major role in the success of ART. They added that future research is required for the mechanism of genetic changes in human embryos and cryopreservation in this field.

## **CONCLUSION**

Reviews from the above articles concluded that assisted reproductive technologies (ART) are an effective treatment including hormonal therapy that stimulates ovulation and intrauterine insemination (IUI), IVF, GIFT, ICSI and other techniques. Literature shows that, although women conceiving through Invitro fertilization have a healthy child higher number of risk factors for both mothers as well as the baby. In mothers, the complications such as ovarian hyperstimulation, hypertensive disorders during pregnancy, increased level of anxiety, ovarian torsion, preeclampsia, placenta previa, placental separation, ectopic pregnancy and most commonly hyperstimulation and multiple pregnancies neurodevelopmental disorders as long-term metabolic outcomes (Gelbaya, 2010; Kathpalia et al., 2016; Sullivan-Pyke et al., 2017). IVF mothers can go for vaginal delivery but should be treated as high-risk labour cases as these mothers need a blood transfusion and intensive care (Kathpalia et al., 2016; Nagata et al., 2019).

IVF therapy become a new hope for infertile couples but at the same time dropout rate from IVF treatment is increasing because of various maternal and perinatal complications. The common rationale given by couples for giving up on ongoing therapy was an economic burden (62.5%), undergoing different methods (6.25%), low ovarian reservoir (25%) and inflammatory bowel disease (6.25%), tension (39%), psychological and physical burden (28%), the anxiety of unsuccessful treatment (13.23%), institutional (11.68%) and clinic (7.71%) (Kulkarni et al., n.d.; Pinborg et al., 2013; S. Gameiro et al., 2012; Verberg et al., 2008). The baby with ART therapy has an increased risk of a major inborn birth defect in terms of the cardiovascular system and chromosomal defects in twins, increased risk of overall cancer in children like leukaemia, and preterm birth (Giorgione et al., 2018a, 2018b; Hargreave et al., 2019).

IVF/ICSI is the step of a procedure which needs very strict observation and experts for its success. It can be possible by an adequate number of skilled IVF specialists and embryologists in our country. Not only quantity but we need proper standardization to carry out more training programs to upgrade our skills and knowledge of ART therapy. In mothers,

the most common complications were hypertensive disorders and multiple pregnancies. Not much study had been done on physical and psychological problems. In terms of IVF child most common diseases associated were congenital heart diseases, neurodevelopmental diseases, birth before completion of gestational age, underweight weight baby, and chromosomal defect. Very least research done on IVF associated with cancer in children so future research can be done on increasing cancer risk in children. India is a developing country people cannot afford IVF treatment because it's expensive so most the couple drop out from the first cycle. The dropout rate may be due to expensive treatment with unexpected outcomes.

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