

# Perinatal Outcome Following Assisted Reproductive Technology in a Tertiary Hospital

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## Abstract

**Objective:** Pregnancies following assisted reproductive technologies have become much more common in tertiary hospitals with neonatal intensive care facilities. The aim of this study is to compare the perinatal outcome of women who conceived through Assisted Reproductive Technologies with who conceived naturally.

**Method:** This retrospective cohort study was conducted in BIRDEM Women and Children Hospital from 1<sup>st</sup> March 2023 to 31<sup>st</sup> March 2024. The study population was divided into two groups. Group 1 was the ART pregnancy (In Vitro Fertilization, IVF) group and Group 2 was the naturally conceived group. The perinatal outcome of two groups of women admitted in the hospital during that period of time for delivery was compared.

**Result:** Mean maternal age of ART pregnancy was 33.89+4.86 years, and 29.26+5.32 years in natural pregnancy. Women with ART pregnancy in comparison to natural pregnancy had statistically significant advanced maternal age (> 35yr) (45/110 Vs 26/130; p=0.001); multiple pregnancy (63.6% Vs <1%, p=0.001) and maternal morbidity [hypertensive disorder of pregnancy (40% vs. 23.85%), hypothyroidism (39.09% vs. 13.58%), premature of rupture of membrane (20.91% vs. 9.23%), preterm labor (20.91% vs. 4.61%), obstetric cholestasis (14.54% vs. 1.54%), chronic placental insufficiency (8.18% vs. 0.0%), breech presentation (8.18% vs. 2.3%) and placenta related morbidities (8.17% vs. 0.76%) (p<0.05)]. Between ART pregnancy and natural pregnancy: mean gestational age at delivery was 33.71+2.36 weeks Vs 36.11+2.29 weeks; preterm births (166/179 Vs 64/131); mean birth weight (2063+557.89 gm Vs 2605gm+649.44gm); low birth weight (70% Vs 33.59%), NICU admission (59% Vs 25.19%). The differences were statistically significant (p=0.001).

**Conclusion:** ART pregnancies have greater perinatal morbidity than naturally conceived pregnancies.

**Keywords:** Perinatal outcome, IVF, pre term birth, low birth weight

## Introduction

Assisted reproductive technologies (ART), is defined by the American Center for Disease Control (CDC) as any fertility-related treatment in which eggs or embryos are manipulated.<sup>1</sup>

IVF is by far the most common ART procedure performed and it is often used as a synonym for ART. But ART procedures may also include intrauterine sperm injection (ICSI), in vitro maturation (IVM), pre implantation genetic diagnosis (PGD),

cryopreservation, surrogacy etc.

The first successful in vitro fertilization (IVF) treatment in human was performed in England in 1978 by Steptoe and Edwards.<sup>2</sup> In the first IVF pregnancy, the woman underwent IVF treatment in a natural cycle with no added ovarian stimulation. A single oocyte was retrieved from the ovary and was then fertilized in vitro. The embryo thus formed was subsequently transferred into the uterus and luckily pregnancy occurred. And thus Louise Brown, a healthy female

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baby was born who is the first IVF baby in the history of humankind.

In the last 40 years, ART has developed tremendously and expanded in access worldwide. The International Committee for Monitoring Assisted Reproductive Technologies estimates that at least 12 million babies have been born as a result of IVF and other assisted reproductive technologies (ARTs) till 2023. <sup>3</sup>

Today, almost all countries in the world have ART facilities to help infertile couples conceive. And Bangladesh is no exception. Currently Bangladesh offers ART facilities mostly in private sectors but also in one Govt. hospital. In addition, a significant number of couples also visit other countries for ART treatment. As a result, number of ART pregnancies has increased significantly specially in a tertiary hospital with neonatal ICU facilities like BIRDEM Women and Children hospital.

With ART being on the up rise, and more children being born as a result, there is more interest in the health outcomes of ART-conceived pregnancies and children. There has been a lot of concern regarding the increased perinatal adverse effects of ART pregnancies like multiple pregnancy and low birth weight. This is even more relevant for a developing country with limited resources like Bangladesh.

So, the present study aims to compare the perinatal outcome of women who conceived through Assisted Reproductive Technologies with who conceived

naturally in BIRDEM Women and Children hospital, Dhaka.

**Methodology:**

This retrospective comparative study was conducted in BIRDEM women and children Hospital from March 2023 to March 2024. BIRDEM women and children hospital is a 152-bedded tertiary hospital with a specialized neonatal intensive care unit. This hospital specializes in high-risk pregnancies including ART pregnancies which are referred here from all over Bangladesh and abroad. The study cohort was divided into two groups. All women who conceived through ART and admitted for delivery during the study period were assigned to group I. Women who conceived naturally were included in Group II. Pregnancies with gestational age less than 22 weeks and all abortions, stillborns and termination of pregnancies were excluded from the study.

Clinical data of the women with neonatal outcome were obtained from the hospital admission registry and medical records. All data were entered into database and this was analysed by SPSS version 23. The perinatal outcome of ART pregnancies was compared with those women and who conceived naturally during that period of time. Descriptive statistics such as mean, standard deviation, range and percentage were used to express data. Differences in two groups were analyzed by Chi-square test. P value < 0.05 was considered as statistically significant.

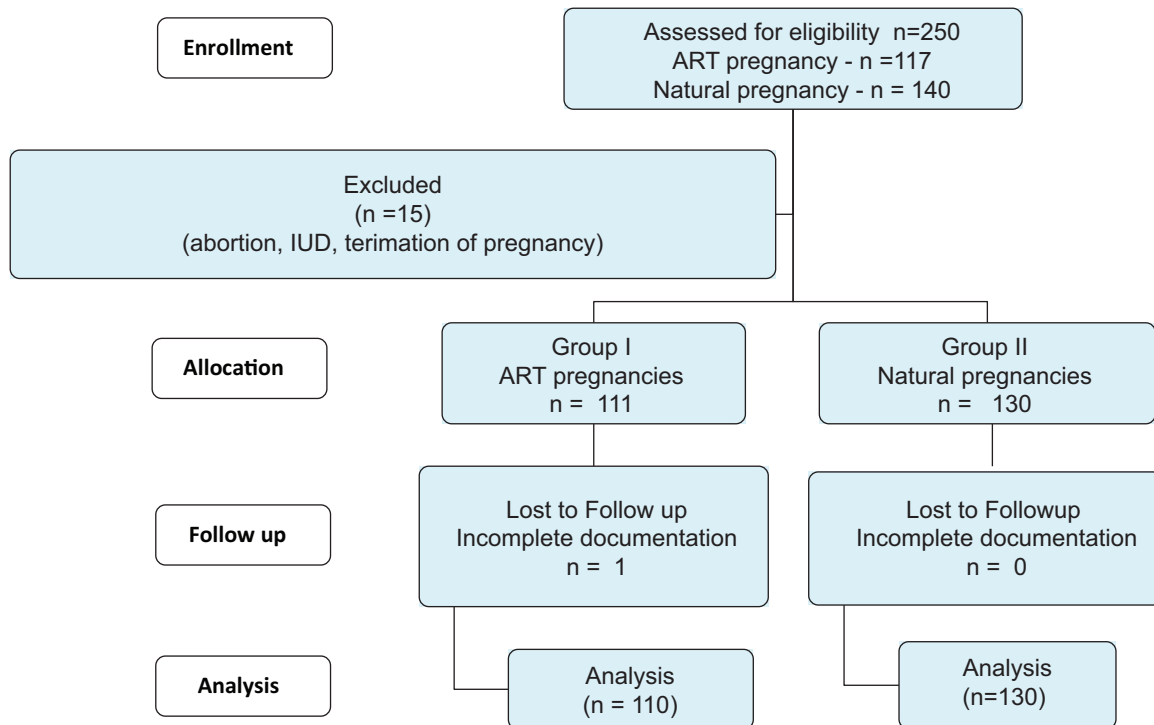
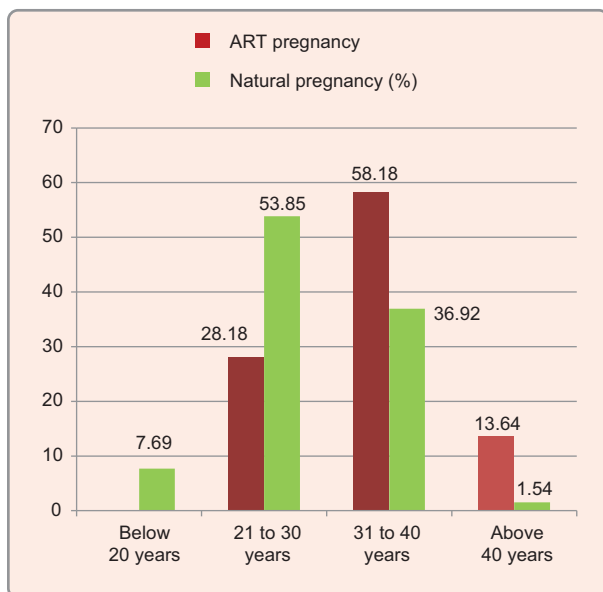


Figure 1: Methodology flow chart

**Result**



**Figure 2:** Distribution of study subjects according to maternal age (percentage).

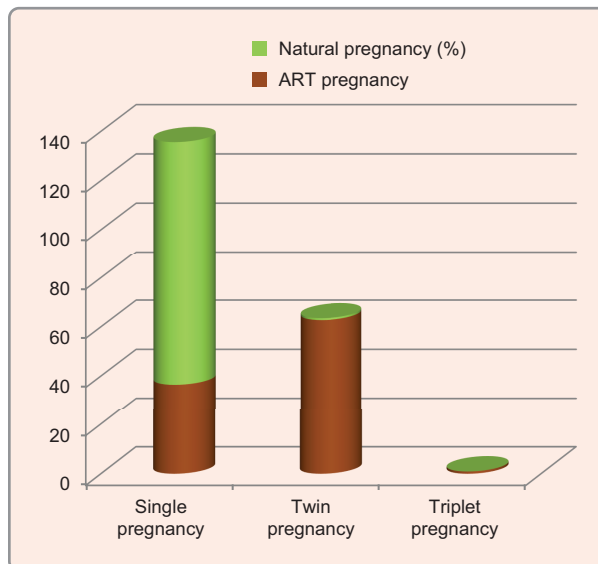
Mean maternal age of ART pregnancy was 33.89+4.86 years (range 24 to 46 years). Mean maternal age of natural pregnancy was 29.26+5.32years (range 18 to 41years).

Women with advanced maternal age (above 35) in ART pregnancy was 45/110 and in natural pregnancy was 26/130. The difference was statistically significant compared between two groups (p=0.001).

Among natural pregnancies 99.23 % (129 / 130) were single pregnancies with only one multiple pregnancy during the study period.

Among ART pregnancies 63.6% (70 / 110) were multiple pregnancies with only 36.4 % (40 / 110) singletons. The difference was statistically significant between two groups (p=0.001).

ART pregnancy had significantly higher in hypertensive disorder of pregnancy (40% vs. 23.85%), hypothyroidism (39.09% vs. 13.58%), premature rupture of membranes (20.91% vs. 9.23%), preterm labor (20.91% vs. 4.61%), obstetric cholestasis (14.54% vs. 1.54%), single fetal demise of twin pregnancy (8.18% vs. 0.0%), chronic placental insufficiency (8.18% vs. 0.0%), breech presentation



**Figure 3:** Distribution of study subjects according to type of pregnancies.

(8.18% vs. 2.3%) and placental cause (8.17% vs. 0.76%) than natural pregnancy (p<0.05).

Mean maternal gestational age of ART pregnancy at delivery was 33.71+2.36 weeks (range 26 to 37 weeks)

Mean maternal gestational age of natural pregnancy at delivery was 36.11+2.29 weeks (range 27 to 44 weeks).

In ART pregnancies, 166 /179 neonates were born preterm whereas 64 /131 neonates in natural pregnancies were born preterm. The difference was statistically significant (p=0.001)

Mean neonatal birth weight in ART pregnancy was 2063+557.89gm (range650gm to 4100 gm). Mean neonatal birth weight in natural pregnancy was 2605gm+649.44 (range 800 gm to 4000gm)

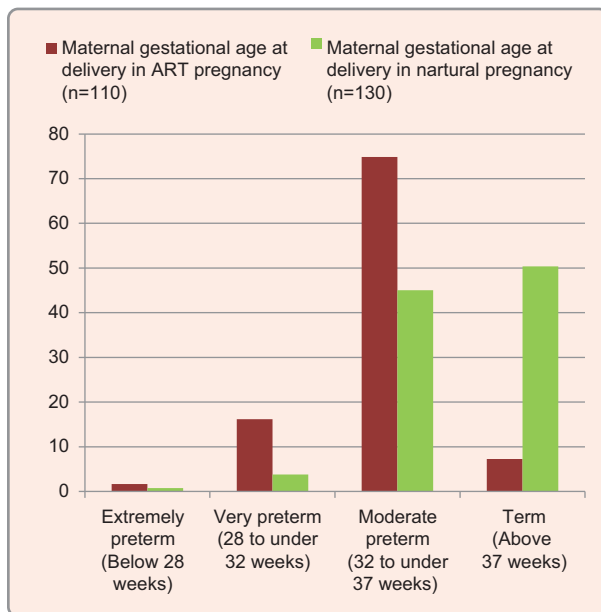
About 142 of 179 neonates (79.33%) were low birth weight babies in ART pregnancies whereas 44 of 131 neonates (33.59%) were born low birth in natural conceptions the difference was statistically significant (p=0.001)

Out of 179 neonates born through ART, 106 were admitted in NICU which was 59.22 %.Out of 131 neonates born through natural conception, 33 were admitted in NICU which was 25.19 %. The difference was statistically significant (p=0.001).

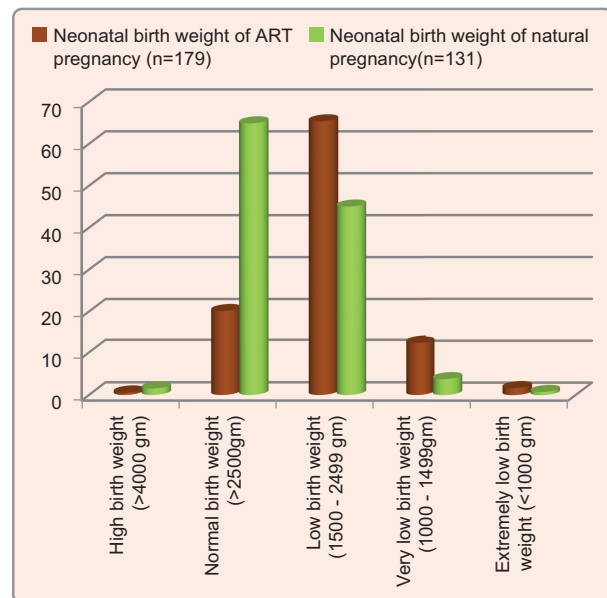
**Table-I**  
*Feto maternal co- morbidities associated with pregnancy*

Type of co morbidity	ART pregnancy (n=110)	Natural pregnancy (n=130)	P value
Hyperglycemia of pregnancy	70 (63.64%)	67 (51.54%)	
a. Gestational DM	46(65.71%)	30(44.76%)	0.059
b. DM- Type II	22(31.43%)	35(52.24%)	
c. DM- Type- I	2(2.86%)	2 (3.0%)	
Hypertensive disorder of pregnancy	44(40%)	31(23.85%)	0.007
a. Pregnancy induced hypertension	21(47.72%)	12(38.71%)	
b. Chronic hypertension	12(27.27%)	12(38.71%)	
c. Pre eclampsia	11(25%)	7(22.58%)	
Hypothyroidism	43(39.09%)	18(13.85%)	0.001
Premature rupture of membrane	23(20.91%)	12(9.23%)	0.010
Preterm labor	23(20.91%)	6(4.61%)	0.001
Obstetric cholestasis	16(14.54%)	2(1.54%)	0.001
Single fetal demise of twin pregnancy	9(8.18%)	0	0.001
Chronic placental insufficiency	9(8.18%)	0	0.001
Breech presentation	9(8.18%)	3(2.3%)	0.037
Placental cause	9(8.18%)	1(0.76%)	0.004
a. Placenta previa	5	1	
b. Morbidly adherent placenta	3	0	
c. Abruption placentae	1	0	
Fetal distress	8(7.27%)	5(3.85%)	0.246
Bad obstetric history	8(7.27%)	17(13.08%)	0.142
Severe oligohydromnios with IUGR	7(6.36%)	7(5.38%)	0.747
Fibroid uterus	6(5.45%)	2(1.54%)	0

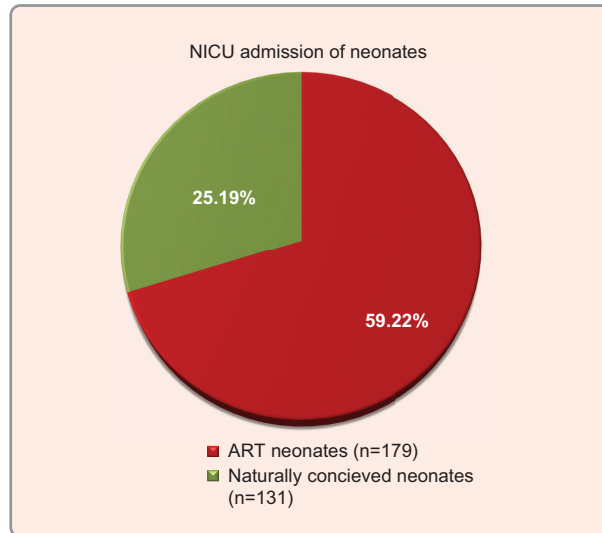
\*Multiple co morbidities were present in most patients.



**Figure 4:** Distribution of study subjects according to gestational age at delivery.



**Figure 5:** Distribution of study subjects according to birth weight.



**Figure 6:** Distribution of study subjects according to neonatal admission to NICU

### Discussion

The present comparative study was conducted to compare perinatal outcome of ART pregnancies with naturally conceived pregnancies at a tertiary care center in Dhaka. From Fig 2 it was observed in our study that mean maternal age of ART pregnancy was  $33.89 \pm 4.86$  years with a range from 24 to 46 years. On the other hand, mean maternal age of natural pregnancy was  $29.26 \pm 5.32$  years with a range of 18 to 41 years. Hadas et al in their study in Israel in 2021 also showed that maternal age at delivery was higher in the IVF pregnancies group compared to natural group ( $32.7 \pm 5.2$  vs.  $29.7 \pm 5.4$  years).<sup>4</sup> In other studies, the results are conflicting. Wenhao et al in their study of perinatal and neonatal outcomes of 494 babies delivered from 972 vitrified embryo transfers found that the mean maternal age was 29.94 with standard deviation 4.08 years which is much lower than our study.<sup>5</sup> But results from a study in Mumbai by Balsarkar and Pol showed similar findings like the present study with a mean maternal age 34.9 years with standard deviation of 5.4 years.<sup>6</sup> Similarly in a study conducted by Nouri et al in Medical University of Vienna, showed that mean age of mother in IVF group was 33.71 with standard deviation 4.92 years.<sup>7</sup> Findings in this study are similar to both above studies.

We also showed that women with advanced maternal age (above 35) in ART pregnancy was 45/110 (40.91%) and in natural pregnancy was only 26/130 (20%). The

difference was statistically significant compared between two groups ( $p=0.001$ ).

Fig-3 showed distribution of study subjects according to type of pregnancies. While 99.23% (129 / 130) of natural pregnancies were single pregnancies with only one multiple pregnancy, 63.6% (70 / 110) ART pregnancies were multiple pregnancies with only 36.4% (40 / 110) singletons. The difference was statistically significant ( $p=0.001$ ). The study by Balsarkar et al showed a different result with 58.3% singletons while a much lower (39.6%) twin pregnancies and 2.1% triplets.<sup>6</sup> In a study by Tallo et al on maternal and neonatal morbidity associated with in vitro fertilization found that of 101 IVF pregnancies, 61.38% were singleton, 35.64% were twins and 2.97% were triplets.<sup>8</sup> Westergaard et al who reported data from the Danish in-vitro fertilization (IVF) registry revealed that 24.3% of their IVF pregnancies were twins and 1.8% triplets.<sup>9</sup> Our results had more multiple pregnancies than singletons in ART pregnancies probably because there is no strict regulation of single embryo transfer in our country and usually 2-3 embryos are transferred per cycle to increase the probability of conception.

Table- 1 showed the list of co morbidities with which the women with both ART and natural pregnancies presented in the study period. Multiple morbidities were present in both groups. As BIRDEM Women and Children hospital is a specialized hospital for management of diabetes mellitus; hyperglycemia was the commonest co morbidity present in both groups followed by hypertension. Both were significantly more in ART group possibly due to advanced maternal age. Hypothyroidism was quite common and significantly higher in ART group. Women in ART group also had more premature rupture of membranes and went into pre term labor more often than natural pregnancies. Presence of underlying pelvic and urinary infection and higher incidence of multiple pregnancies may be the cause. Obstetric cholestasis was alarmingly high in ART group as well. The study by Balsarkar also revealed hyperglycemia, hypertensive disorder, hypothyroidism and placental abnormalities as the leading co morbidities in women with IVF pregnancies.<sup>6</sup> Asbagh et al in Tehran found that GDM was obstetrics complication in 6% study participants, pre-eclampsia in 2%, placenta previa in 4% and placental abruption in 2%.<sup>9</sup> Findings of our study are similar to the above mentioned studies in terms of obstetric complications of the mother. Regarding the fetal

conditions, malpresentation (probably due to prematurity), chronic placental insufficiency with intra uterine growth restriction and fetal distress were more common in ART pregnancies in our study. Higher rate of single fetal demise of a twin pregnancy was also a significant finding in this study.

As our hospital is a tertiary referral center with excellent neonatal ICU facilities, high risk pregnant women needing preterm delivery are mostly referred here. So, this study revealed that majority of both groups of women delivered pre term with mean maternal gestational age of ART pregnancy at delivery was 33.71+2.36 weeks (range 26 to 37 weeks) in comparison to natural pregnancy which was 36.11+2.29 weeks (range 27 to 44 weeks). (Fig:4). The study result differed from results from Israel (Hadas et al) where the rate of preterm labor, hypertensive disorders of pregnancy and intrauterine growth restriction were similar between the two groups.<sup>4</sup>

In this study, the mean neonatal birth weight in ART pregnancy was 2063+557.89gm (range 650gm to 4100 gm) in comparison to 2605gm+649.44 (range 800 gm to 4000gm) in natural pregnancy. It was also revealed that 142 of 179 neonates (79.3%) were low birth weights (LBW) babies in ART pregnancies whereas 44 of 131 neonates (33.59%) were LBW in natural conceptions (Fig-5). The difference was statistically significant when compared between two groups ( $p=0.001$ ). In the Balsarkar study, mean weight of newborn children was 1800 gm with Standard deviation 860 kgm.<sup>6</sup> Chung et al found that mean birth weight was 2118 gm with standard deviation 605 gm in their study.<sup>10</sup> In Talle study, the mean birth weight was 2623 gm with standard deviation 0857 gm.<sup>8</sup> The birth weight of IVF neonates in this study were much lower than above mentioned studies and this may be due to the difference in socio demographic profile of study participants and also due to the increased incidence of multiple pregnancies. But this study found 1.68% extremely low birth weight and 12.29% very low birth weight babies in ART group which is much lower than 17.8% extremely low birth weight new born and 17% very low birth weight neonates in the Talle study.

In the present study, 106 out of 179 neonates born through ART were admitted in NICU which was 59.22%. Whereas 33 out of 131 naturally conceived neonates were admitted in NICU which was 25.19%. The difference was statistically significant compared between two groups ( $p=0.001$ ). (Fig-6)

## Conclusion

Infertile couples all over the world including Bangladesh are greatly benefited through ART but this study is an eye-opener to the adverse perinatal outcomes of ART pregnancies and its financial outcome. This study will help the clinicians to take further steps to reduce the alarming perinatal outcomes and it will also help the infertile couples to calculate the risk benefit ratio of ART treatments. Further long term studies are required to reveal the long-term outcome of ART neonates in comparison to naturally conceived neonates.

## Limitations

As it a single hospital based study with a small sample size, findings cannot be generalized to the whole population.

**Conflict of interest-** None

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