



## Adverse Fetomaternal Outcomes in Women Who Received Various Infertility Treatments before Conception

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### ABSTRACT

**Background:** Growing number of hormonal reproductive technique and assisted reproductive techniques are being employed to couples presenting for infertility. However, the outcomes of these techniques have seldomly been reported from our population and majority of the data comes from international studies, the results of which cannot be generalized. Hence it is important to have knowledge about outcomes in local population. Hence the study has been planned. Results of my study will enable obstetricians in better counselling of the regarding fetomaternal outcomes in patients receiving infertility treatments. **Objective:** To determine the frequency of various fetomaternal outcomes in patients with infertility treatments and compare hormonal treatment and assisted reproductive technique. **Methods:** This descriptive study was carried out at the department of Obs and Gynae, KTH, Peshawar during the period from November 2024 to April 2025. Patients aging 20 to 40 years, with gestational age more than 20 weeks with history of hormonal or assisted reproductive technique on medical record were enrolled. Patients were evaluated for fetomaternal outcomes. **Results:** The mean age of the participants was  $30.49 \pm 5.528$  years and 77 patients (51.3%) were aging more than 30 years. 68 participants (45.3%) had received hormonal treatment and 82 (54.7%) had assisted reproductive techniques. Still birth was recorded in 9 patients (24.3%) with hormonal treatment compared to 28 (75.7%) with ART ( $p = 0.003$ ). Low Apgar was more common with hormonal treatment ( $n = 18, 66.7\%$ ) compared to 9 (33.3%) with ART ( $p$  value 0.014). PPH was more frequent with ART ( $n = 21, 72.4\%$ ) compared to 8 (27.6%) with hormonal treatment ( $p$  value 0.033). **Conclusion:** Fertility treatments including hormonal and ART are associated with a variety of maternal and postnatal problems. Some of the primary reasons for this might be the advanced age of the women who opt for it, the lack of conception history among these individuals, and the associated high-risk variables.

### INTRODUCTION

Approximately 200 million people worldwide suffer from infertility, which has led to a substantial need for reproductive procedures. IUI and IVF are among the most popular assisted reproductive techniques (ART), alongside roughly twenty-five million sessions of treatment carried out annually worldwide, producing over 500,000 babies. ART includes processes including the laboratory managing human eggs and sperm or embryo.<sup>1</sup>

According to investigations, there are higher chances to have multiple newborns, premature births, lower birth weights, stillbirths, augmentation of labor, and deliveries by cesarean section after ART than in naturally formed conceptions.<sup>2</sup> ART has additionally been linked to infant death, hospitalization to neonatal ICU, and poor Apgar scores. Nevertheless, there are few studies assessing pregnancy and infant health consequences following non-

ART fertility procedures. The majority of ART studies to date have categorized kids raised following non-ART fertility procedures (hormonal medications and insemination) as spontaneously conceived infants and have concentrated on the risks of ART alone.<sup>3,4</sup>

Research on the long-term wellbeing of infants born using assisted reproductive technology indicates that such children grow properly and are typically healthy. According to comprehensive evaluations, there was no discernible difference between ART-treated and naturally generated children's general growth. In the UK, a nationwide cohort study of children on ART revealed early development characteristics like those of infants conceived naturally. 5, 6 Congenital deformities, genetic abnormalities, increased medical service utilization, and longer hospital stays have all been linked to conception using ART, according to some data. 7. Although hereditary

traits and lifestyle variables may have influenced the results, long-term follow-up studies have shown an increased risk of cardiovascular illnesses, diabetes, and several types of cancer.<sup>8</sup>

In a study the proportion of still birth is patients who received ART was 6.63% and 4.84% in patients who received hormonal induction. Preterm birth was recorded for 22.0% infants with ART and 14.8% infants born through induction technique. Low Apgar was recorded in 2.9% infants in ART group and 2.9% patients with hormonal treatment induction. Caesarean delivery was recorded for 48.8% women with ART and 36.6% patients with hormonal induction technique.<sup>6</sup>

Growing number of hormonal reproductive technique and assisted reproductive techniques are being employed to couples presenting for infertility. However, the outcomes of these techniques have seldomly been reported from our population and majority of the data comes from international studies, the results of which cannot be generalized. Hence it is important to have knowledge about outcomes in local population. Hence the study was planned to determine the frequency of various fetomaternal outcomes in patients with infertility treatments and compare hormonal treatment and assisted reproductive technique. Results of my study would enable obstetricians in better counselling of the regarding fetomaternal outcomes in patients receiving infertility treatments.

## MATERIALS AND METHODS

This descriptive study was carried out at the department of Obs and Gynae, KTH, Peshawar during the period from November 2024 to April 2025. Patients aging 20 to 40 years, with gestational age more than 20 weeks with history of hormonal or assisted reproductive technique on medical record were enrolled. Patients were evaluated for fetomaternal outcomes. Patients with hormonal disorder, contracted pelvis, fetal anomalies and placenta previa were excluded. Infertility treatments were defined as 1) Hormonal treatment: Pregnancy conceived through the use of agents that stimulate the development and release ovum such as letrozole, gonadotropins or clomiphene and 2) Assisted reproductive technique: Pregnancy conceived through fertilizing partner ovum outside her body with the sperm of the husband in a controlled environment of a specialized laboratory and then implanting the embryo in the uterus. Fetal outcomes were measured as low Apgar (Apgar score less than 7 at 5 minute after birth, still birth (baby born with no signs of life after 20 weeks of gestation) and preterm birth (baby born prior to 37 weeks of gestation). Maternal outcomes included mode of delivery (normal vaginal delivery or caesarean delivery) and postpartum hemorrhage (loss of more than 500ml blood after NVD and more than 1000ml after caesarean delivery measured using kidney tray (1 kidney tray = 500ml). Sample size was 150, calculated using WHO sample size formula taking anticipated proportion of caesarean delivery after assisted reproductive technique=48.8%<sup>6</sup>, margin of error = 7.5% and confidence level= 95%. Sampling technique was non probability consecutive sampling.

Approval was sought from hospital IRB, following which participants were enrolled. Informed consent was obtained. Baseline information and demographics were noted. Medical record was reviewed. Hormonal or assisted reproductive technique was noted. Medical examination was carefully performed followed routine labs. Patient were closely followed up at 2 weeks interval till 30 weeks of gestation and weekly thereafter till delivery. For delivery patient were admitted into labour room. Gestational age at the time of delivery, mode of delivery, blood loss, birth status of baby and apgar score was recorded.

Data was analyzed using statistical analysis program IBM SPSS version 25. Means  $\pm$  SD or median (IQR) was recorded for quantitative data like age, weight, height, BMI, gestational age and blood loss after checking the normality of the data by Shapiro wilk test. Frequencies and percentages were recorded for qualitative data like parity, treatment modality (hormonal/ART), residence, education, profession, SE status, fetal and maternal outcomes. Both groups (hormonal/ART) were compared for fetal and maternal outcomes by applying chi square or fisher exact test at 5% level of significance. Fetal and maternal outcomes were stratified by age, BMI and parity to control the effect modifiers. Post stratification chi square test or fisher exact test at 5% level of significance was applied.

## RESULTS

The mean age of the participants was 30.49 $\pm$ 5.528 years, mean gestational age was 34.37 $\pm$ 4.890 weeks and mean BMI was 23.976 $\pm$ 2.601 kg/m<sup>2</sup> as reported in table 1.

**Table 1**

*Descriptive statistics of study participants (n = 150)*

Parameters	Mean	Std. Deviation
Age (years)	30.49	5.528
PoG (weeks)	34.37	4.890
BMI (kg/m <sup>2</sup> )	23.976	2.6018

77 patients (51.3%) were aging more than 30 years and 98 participants (65.3%) had BMI less than 25.0kg/m<sup>2</sup>. Parity more than 3 was recorded in 71 patients (47.3%). 68 participants (45.3%) had received hormonal treatment and 82 (54.7%) had assisted reproductive techniques as shown in table 2.

**Table 2**

*Distribution of Study Participants according to Various Parameters (n = 150)*

Parameters	Subgroups	Frequency	Percent
Age (years)	30 or below	73	48.7
	Above 30	77	51.3
BMI (kg/m <sup>2</sup> )	less than 25.0	98	65.3
	25.0 or above	52	34.7
Parity	3 or below	79	52.7
	More than 3	71	47.3
Education	Yes	59	39.3
	No	91	60.7
Mode of Rx	Hormonal	68	45.3
	ART	82	54.7

Still birth was recorded in 9 patients (24.3%) with hormonal treatment compared to 28 (75.7%) with ART. The p value for difference was 0.003. Low Apgar was more common with hormonal treatment (n = 18, 66.7%) compared to 9 (33.3%) with ART (p value 0.014). Preterm delivery was recorded in 23 patients (42.6%) with hormonal treatment compared to 31 (57.4%) with ART with p value 0.613. PPH was more frequent with ART (n = 21, 72.4%) compared to 8 (27.6%) with hormonal treatment (p value 0.033) as shown in table 3.

**Table 3**

*Fetomaternal Outcomes with Respect to Mode of Treatment (n = 150)*

		Mode of Treatment		Total	P value
		Hormonal (n = 68)	ART (n = 82)		
Still Birth	Yes	9 24.3%	28 75.7%	37 100.0%	0.003
	No	59 52.2%	54 47.8%	113 100.0%	
Low Apgar	Yes	18 66.7%	9 33.3%	27 100.0%	0.014
	No	50 40.7%	73 59.3%	123 100.0%	
Preterm	Yes	23 42.6%	31 57.4%	54 100.0%	0.613
	No	45 46.9%	51 53.1%	96 100.0%	
PPH	Yes	8 27.6%	21 72.4%	29 100.0%	0.033
	No	60 49.6%	61 50.4%	121 100.0%	
Mode of delivery	CS	31 44.3%	39 55.7%	70 100.0%	0.809
	NVD	37 46.3%	43 53.8%	80 100.0%	

## DISCUSSION

Therapy is becoming a more popular field of science owing to the growing prevalence of infertility. A quicker rhythm of existence, more work-related stress, deteriorating environmental quality, postponed wedding, and older ages initially pregnancy are all contributing factors to a rise in the incidence of infertility.

Majority of the patients were aging more than 30 years in our cohort of patients. Our results were comparable to a research conducted by Luke B et al, which found that the average age of women pregnant by ART remained 32.53 years. In their research, 63.3% were singlets and 36.3% had twins.<sup>9</sup> This is explained by the usage of single transfer of embryos in in vitro fertilization nowadays. The primary cause is to circumvent several pregnancy problems.

The main issue encountered in our research was preterm labor. According to Gao et al., fertility treatment fertilization was linked to kids that were tiny for

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gestational age, had low birth weights, and were delivered prematurely.<sup>10</sup> Both the Jie Z et al. ART group and IVF/ICSI pregnancies had greater incidences of premature birth and other complications.<sup>11</sup> Wang AY et al. discovered that 82% of ART patients had cesarean sections.<sup>12</sup>

Equivalent but somewhat lower rates were found in this investigation. 40% of our patients were delivered vaginally, and 60% underwent caesarean sections. A majority of women choose elective caesarean sections over vaginal birth because the pregnancy is valuable after protracted infertility. Adverse birth outcomes are linked to more than one pregnancy, which are more prevalent with ART babies. In order to decrease the number of pregnancies, several nations employ elective single embryo transfers (e SET) and extra cycles using stored or thawed embryos.<sup>13</sup>

According to available data, nonetheless single ART pregnancies carry a higher risk. ART promotes adverse consequences for multiple, unidentified reasons. The fundamental fertility problems diagnosis of women using ART may have negative effects. ART may cause damage to ART children, particularly growing embryos and cold storage. Perinatal effects are also impacted by ovarian excessive stimulation.<sup>14</sup> This study looked at infant fatalities, stillbirths, neonatal ICU admissions, and Apgar scores at five minutes. The 5-minute Apgar score and its variation from 1 to 5 minutes can be used to evaluate resuscitation progress.

Neonatal neurotoxicity was not brought on by peripartum hypoxia or ischemia, as evidenced by the 24% of infants that achieved Apgar score 7 or above at 5 minutes. 9.76% received a score below 7. Daniel Y et al. found that ART newborns were more likely than spontaneous babies to have low 5th-minute Apgar scores (<7).<sup>14</sup> According to Pourali L et al., there was no discernible difference in Apgar score spontaneous conception and ART. This might be explained by fewer instances of premature births.<sup>15</sup>

## CONCLUSION

Fertility treatments including hormonal and ART are associated with a variety of maternal and postnatal problems. Some of the primary reasons for this might be the advanced age of the women who opt for it, the lack of conception history among these married individuals, and the associated high-risk variables. Couples undergoing ART as a technique of conception should get counseling to lower these risks. Despite the notion that ART is a last choice for couples who have exhausted all other alternatives for treating infertility.

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