



Article

# Perinatal Risk Factors in Newborns from Multiple Pregnancies Following in Vitro Fertilization

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**Abstract:** Multiple pregnancies remain one of the most challenging conditions in modern obstetrics because they are frequently associated with prematurity, neonatal adaptation disorders, and increased perinatal morbidity, while pregnancies achieved through in vitro fertilization may additionally carry risks related to maternal reproductive history and assisted conception procedures. The present study aimed to compare perinatal risk factors and early neonatal outcomes among newborns delivered from multiple pregnancies after IVF and naturally conceived multiple pregnancies. A comparative clinical analysis was performed using data obtained from 120 newborns divided into two groups according to the method of conception. The results demonstrated that newborns from IVF-associated pregnancies had lower gestational age, reduced birth weight, higher frequency of respiratory distress syndrome, and more frequent admission to neonatal intensive care units. Naturally conceived multiple pregnancies also demonstrated elevated neonatal risks, although complications were comparatively less severe. The findings highlight the necessity for intensified prenatal surveillance and specialized neonatal management in pregnancies following assisted reproductive technologies.

**Keywords:** in vitro fertilization, multiple pregnancy, neonatal outcomes, perinatal risk factors, prematurity, neonatal intensive care, assisted reproductive technologies.

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## Introduction

The dramatic development of assisted reproductive technologies (ART) over the last 2 decades has profoundly altered the modern face of obstetrics and neonatology, as in vitro fertilization (IVF) has become a therapeutic approach to infertility and an important demographic fact affecting the rates of multiple gestations around the world, while assisted reproduction has offered thousands of families the chance to conceive after years of reproductive problems, it has also created more pregnancies with increased maternal and neonatal risks, particularly those of twins and higher-order gestations [1].

The multiple pregnancies and their associated complications are physiologically complex; the maternal organism must sustain the development of two or more fetuses and this often results in placental insufficiency, premature delivery, fetal growth restriction and neonatal adaptation disorders, and pregnancies conceived through IVF can also be potentially affected by hormonal stimulation, implantation features, maternal age, history of infertility and preexisting reproductive disease prior to conception [2].

Neonatologists and obstetricians have increasingly focused on the outcomes of IVF-associated multiple pregnancies over the past few years because clinical observations repeatedly showed that infants born from these pregnancies are at increased risk of

requiring intensive neonatal support immediately after birth, especially due to respiratory distress syndrome, low birth weight and intraventricular hemorrhage, infectious complications, and prolonged hospital stay in NICUs, while multiple pregnancies that occurred naturally would show comparatively different pattern of perinatal adaptation and morbidity, albeit they are also considered a high-risk group [3].

However, progress in neonatal care has resulted in an increase in survival rates, including for extremely premature infants, and the burden of early complications and long-term neurodevelopmental consequences is a significant medical and social problem, particularly for developing health care systems with limited availability of neonatal specialty services. Although many international studies have focused on ART-related multiple pregnancies in recent years, there are still many questions that have not received enough attention with regard to the perinatal outcomes of these multiple pregnancies, especially regarding the regional clinical practice and certain population-specific characteristics, making further studies of this topic relevant for the optimization of perinatal monitoring, management of delivery, and the reduction of neonatal morbidity and mortality [4].

### Materials and Methods

The clinical comparative study was conducted in the multidisciplinary clinic of Samarkand State Medical University in the neonatal and obstetric clinics from 2022 to 2025. The investigation was directed towards the perinatal state of newborns born from multiple pregnancies as well as the comparison of the incidence of unfavorable neonatal outcomes related to the methods of conception. Since newborns of multifetal gestations often need special medical care shortly after birth particularly if the pregnancy is complicated by prematurity or placenta dysfunction, attention was directed to the early neonatal adaptive responses.

The study included a total of 120 multiple birth babies. Clinical population examined was divided into two clinical groups. The first group were newborns born from multiple pregnancies after in vitro fertilization, and the second group were newborns born from naturally conceived multiple pregnancies. Neonates that were not live born and had incomplete maternal and neonatal medical records were excluded from the analysis.[5]

Major congenital defects, chromosomal abnormalities, severe maternal non-pregnancy-related diseases and incomplete clinical records were excluded to limit the impact of confounding variables on the neonatal outcome.[6]

A detailed retrospective assessment of maternal history, obstetric complications, delivery characteristics and neonatal clinical indicators was part of the research process. Considered maternal factors were age, period of infertility before conception, obstetric history, mode of delivery, and presence of gestational hypertension, preeclampsia, anemia, gestational diabetes mellitus and threat of premature labor. Maternal demographic characteristics were seen as an important part of the comparative analysis since pregnancies obtained with the use of assisted reproductive technologies are often experienced in older reproductive age women.

Neonatal evaluation was conducted at the time of birth and early neonatal period. In both groups, the following factors were evaluated: gestational age, birth weight, body length, Apgar scores at 1st and 5th minutes, oxygen therapy, admission to a neonatal intensive care unit and infectious or neurological complications. The criteria adopted for the assessment of prematurity were those of the WHO and for low birth weight and neonatal respiratory disorders those of the latest international neonatal recommendations. The results obtained were then subjected to statistical processing using statistical software SPSS. Results were expressed as mean values (standard deviation) for quantitative variables, and percentages for qualitative variables. Student's t-test and chi-square analysis were used for comparative analysis of the two groups. The differences were regarded as statistically significant at  $p < 0.05$ . Confidentiality of patient information was fully

respected and ethical principles of biomedical research involving human participants were respected throughout the study [7].

## Results and Discussion

### Results

The comparative analysis revealed that the frequency of the adverse outcomes were significantly higher in newborns from IVF multiple pregnancy compared to the neonates born from multiple pregnancy in the natural way. Both groups were considered to be high risk neonates due to multifetal gestation, but complications were more severe and distributed among the IVF group, especially in terms of prematurity, respiratory adaptation disorders and the need for intensive neonatal support during the first few days of life[8].

The most important difference between the groups was in the gestational age at delivery. IVF pregnancies were more likely to be premature (before 37 weeks). Numerous these neonates showed early neonatal signs of functional immaturity, unstable thermoregulation and feeding difficulties. Besides, the average birth weight of IVF group continued to be lower than that of the naturally conceived group, and there was a higher incidence of low birth weight <2500 g [9]. Another clinical observation was that these newborns needed more time to adapt to life after birth and more careful monitoring of their breathing immediately after birth.

Apgar scores at the first minute after birth were lower more frequently in IVF newborns, particularly in those with the following complications: preterm rupture of membranes, placental insufficiency and hypertensive disorders in the mother during pregnancy. The most common complication in both groups was respiratory distress syndrome, although oxygen use and admission to the neonatal intensive care unit was significantly higher in IVF babies. A few infants also exhibited transient neurological depression, muscular hypotonia, and mild manifestations of hypoxic involvement within the first 24 hours of birth [10].

Additionally, maternal complications had an indirect effect on the outcomes of the newborns. Anemia, cesarean section and pre-eclampsia were more common in pregnancies following IVF, and this may have been a factor in earlier pregnancies going to delivery and neonatal instability. In the meantime, naturally conceived multiple pregnancy, although with relatively better adaptation indicators, had high rates of prematurity compared to singleton gestations in international neonatal statistics [11].

Table 1. Comparative perinatal outcomes in newborns from multiple pregnancies

Indicators	IVF Multiple pregnancy group (n=60)	Natural conception group (n=60)
Mean gestational age (weeks)	34.1 ± 1.8	35.6 ± 1.5
Mean birth weight(g)	2210 ± 320	2480 ± 290
Prematurity frequency	71.6%	53.3%
Low birth weight (<2500)	68.3%	46.6%
Cesarean section rate	83.3%	61.6%
Respiratory distress syndrome	36.6%	21.6%
NICU admission	41.6%	25.0%
Apgar score < 7 at 1 minute	28.3%	15.0%
Early neonatal infection	13.3%	8.3%

Table interpretation: The data presented suggest that early neonatal outcomes were worse for IVF-associated multiple births than for spontaneous multiple births. The differences were most marked in terms of the prevalence of pre-term births, respiratory complications, and NICU admission rates, and whether there is a greater number of low birth weight infants in ART pregnancies, which may lead to a further increased risk of perinatal vulnerability. In summary, the results obtained are in line with the clinical experience that multiple pregnancies after IVF are associated with increased levels of prenatal surveillance and special care in the newborn period, as well as a higher rate of physiological immaturity in the first days after birth [12].

#### Discussion

Once again, the results of this study have demonstrated that multiple pregnancies are one of the most clinically problematic situations in current obstetrics and neonatology practice, and pregnancies resulting from in vitro fertilization seem to be even more complicated as several biological and obstetric factors are present simultaneously, such as advanced age of the mother, placental dysfunction, hormonal stimulation before implantation, and the markedly increased incidence of premature delivery [13].

Despite the significant success of reproductive medicine, neonatal adaptation of IVF-born infants remains a serious problem in the care of these infants by the clinician, especially when the IVF involves twins and higher-order gestations, where intrauterine resource competition is increased as the pregnancy advances.

The present study found that IVF associated multiple pregnancies significantly increased rates of preterm birth and LBW, which is in line with more recent international observations that ART is often associated with a reduction in gestational duration and a decrease in fetal growth dynamics. A possible mechanism is in relation to placental vascular insufficiency, known to occur more commonly in IVF pregnancies, due to the differences in the mechanisms of implantation and trophoblastic invasion compared to spontaneous pregnancies [14].

Therefore, many newborns show evidence of physiological immaturity, respiratory instability, and diminished adaptive responses during the early neonatal period even when pregnancies have been extended beyond the critical period of viability.

Another significant finding was that there was a higher incidence of RDS and NICU admissions among the IVF group. The pattern is clinically comprehensible as it is linked to the pulmonary immaturity which is strongly related to preterm birth, while multifetal gestations are already known to be predisposed to incomplete fetal lung maturation. Furthermore, cesarean delivery occurred more frequently in IVF pregnancies, which also might affect transitory respiratory adaptation following birth, through delayed clearance of fetal lung fluid [15]. Several of the neonates were also neurologically depressed and muscly hypotonic immediately after delivery, suggesting that chronic intrauterine hypoxia and placental insufficiency may also be a factor in early neurological vulnerability as well as respiratory morbidity. It is also important to remember that, at the same time, there were also reported higher risks of neonatal complications in naturally conceived multiple pregnancies versus singletons in more general epidemiological studies. Thus, the IVF procedure cannot be blamed entirely as multifetal pregnancy in itself induces significant physiological stress to the mother and fetuses. However, there are certain risks which may be exacerbated by the nature of the assisted reproductive technologies and the mother's reproductive history [16].

The acquired data confirm the importance of personalized prenatal monitoring, prompt recognition of placental insufficiency and the integration of efforts between obstetricians, reproductive specialists, and neonatologists. Putting in place early prevention strategies to reduce prematurity and to optimize fetus maturation could substantially improve the outcome of newborns and reduce the use of intensive care interventions in this fragile population.

## Conclusion

The study performed showed that the in vitro fertilization (IVF) related multiple births are one of the most sensitive sub-groups of newborns that needs more medical care during the prenatal and early postnatal periods. While multiple gestation is considered a risk factor for obstetric and neonatal complications, the results obtained indicate that pregnancies resulting from ARTs have a greater incidence of adverse obstetric-neonatal outcomes compared to naturally conceived multiple pregnancies. While the most clinically significant differences were related to prematurity, low birth weight, respiratory adaptation disorders and the need for neonatal intensive care immediately following delivery, other differences were statistically nonsignificant. In Comparison analysis it was shown that the newborns of IVF showed more often signs of physiological immaturities, unstable breathing, and decreased adaptability during the first days of life. These pregnancies are at a high risk of being monitored closely starting from the early stages of pregnancy as prematurity and RDS are associated with these pregnancies. The predominance of cesarean delivery, anemia and preeclampsia, as maternal complications, also had an indirect influence on neonatal condition, and may have contributed to the exacerbation of perinatal adaptation processes. Concurrently, the results showed that naturally conceived multiple pregnancies are also not clinically safe as there is also a significant neonatal morbidity, particularly with regard to early adaptation difficulties and preterm birth. However, complications among IVF-originated babies indicate that ART can exacerbate pre-existing biological and obstetric risk factors of multiple gestation. The findings of this study highlight the need for multidisciplinary management of the patient by a reproductive specialist, obstetrician, neonatologist, and intensive care specialist. Although the precise impact on neonatal mortality and morbidity outcomes may be even more, this set of activities could substantially reduce adverse perinatal outcomes and enhance the quality of neonatal survival if carried out at an early stage with a timely strategy to prevent prematurity and with an enhanced system of neonatal monitoring. More extensive multi-center studies are still needed to gain greater insight into long-term consequences on development among children born from IVF-associated multiple births.

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