

## Abstract

Data is lacking regarding outcomes for preterm infants following in-vitro fertilization (IVF) assisted conception. We aimed to elucidate potential concerns for increased complications and adverse neurodevelopmental outcomes for preterm infants conceived via IVF. In-hospital and neurodevelopmental data were similar between study patients and controls, providing reassurance to individuals considering IVF.

## Introduction

Infants conceived with IVF account for ~1.6% of live births in the United States. IVF is associated with an increased risk of low birth weight, multifetal gestation, and preterm birth. The Centers for Disease Control and Prevention (CDC) classifies preterm birth into 3 categories: overall preterm (<37 weeks gestational age - GA), moderately preterm (between 32-36 weeks GA) and very preterm (<32 weeks GA). Outcomes for full-term infants from reproductive endocrinology and infertility (REI) assisted conception practices such as IVF have been well reported, but there remains a paucity of data focused on outcomes of preterm IVF infants. We hypothesize that preterm infants conceived via IVF may have different inpatient and neurodevelopmental outcomes in comparison to preterm infants with unassisted conceptions.

## Objective

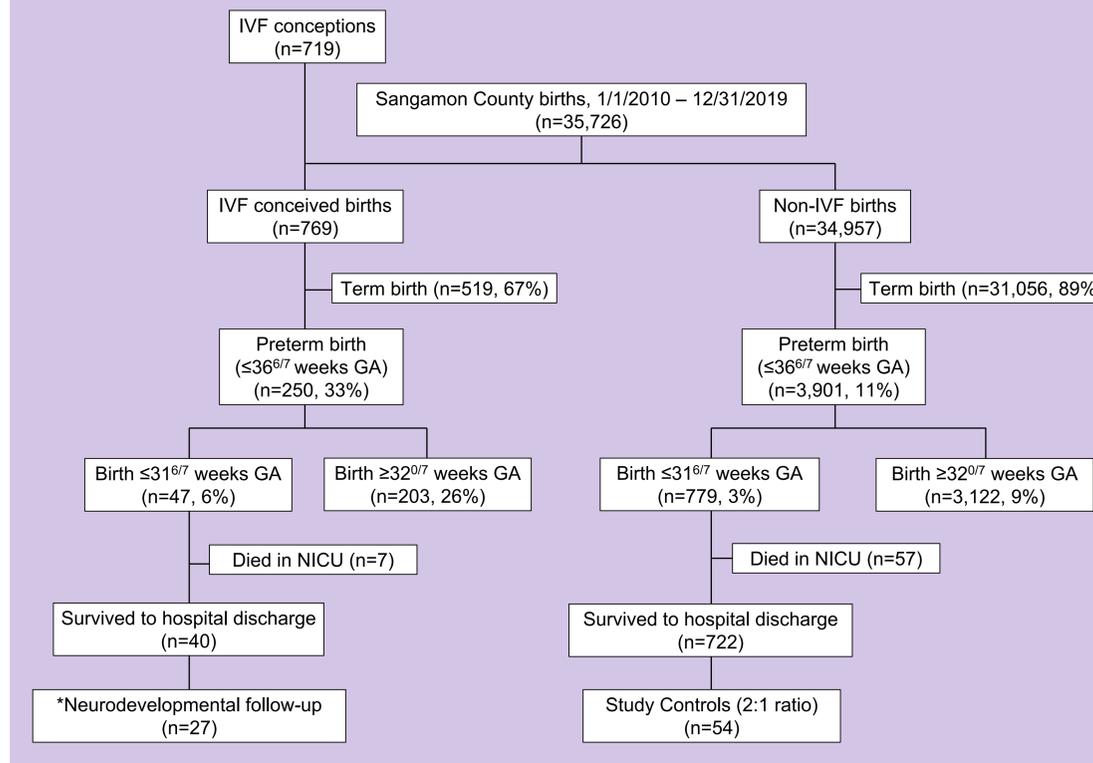
This retrospective review aims to describe inpatient demographics, complications (e.g., bronchopulmonary dysplasia, necrotizing enterocolitis) and neurodevelopmental outcomes for a large single center cohort of preterm infants conceived via IVF between January 1, 2010 and December 31, 2019.

## Methods

- Infants conceived via IVF who were born <31<sup>6/7</sup> weeks GA who survived until Neonatal ICU discharge were matched 2:1 to control patients based on GA, birth weight and gender. All patients were cared for in the Neonatal ICU at HSHS St. John's Hospital.
- In-hospital and neurodevelopmental (ND) outcome data (Bayley Infant Neurodevelopmental Screener [BINS]) for the two cohorts were analyzed.
- T-tests and chi-square tests were used to analyze continuous and categorical outcomes, respectively.

## Results

**Figure 1: Births in Sangamon County over a Ten-Year Period**



**Table 1: Demographic and Preterm Infant Outcome Data**

	IVF Patients (n=27)	Control Patients (n=54)	P value
Maternal age, mean ± SD	32.4 ± 5.9	28 ± 4.6	0.002
Primigravida, # (%)	12 (44.4%)	25 (46.3%)	0.875
Race / ethnicity:			0.99
Caucasian, # (%)	26 (96.3%)	52 (96.3%)	
African-American, # (%)	1 (3.7%)	2 (3.7%)	
Rural residence, # (%)	10 (37.0%)	21 (38.9%)	0.87
Antenatal corticosteroids, # (%)	13 (48%)	34 (63%)	0.20
Gestational age (weeks), mean ± SD	28.6 ± 2.1	28.7 ± 2.1	0.59
Birth weight (grams), mean ± SD	1214 ± 357	1257 ± 325	0.33
Cesarean, # (%)	21 (77.8%)	40 (74.1%)	0.72
Surfactant, # (%)	9 (33%)	33 (61.1%)	0.009
Severe intraventricular hemorrhage, # (%)	0 (0%)	3 (5.6%)	0.19
Survival to NICU discharge, # (%)	27 (100%)	54 (100%)	1.00
Bronchopulmonary dysplasia, # (%)	7 (25.9%)	8 (14.8%)	0.23
Necrotizing enterocolitis, # (%)	0 (0%)	3 (5.6%)	0.21
Severe retinopathy of prematurity, # (%)	1 (3.7%)	1 (1.9%)	0.61
Postnatal growth (gm/day), mean ± SD	25.5 ± 15.6	24.5 ± 8.1	0.74
Length of Stay (days), mean ± SD	66.5 ± 36.6	64.3 ± 29.2	0.65

There were 719 IVF conceptions during the 10-year study period with 769 live-births, including 519 (67%) term births and 250 (33%) preterm births of whom 47 (6%) were born <31<sup>6/7</sup> weeks GA. Of these 47 infants, seven died in the NICU and 13 were lost to follow-up. The remaining 27 infants were matched to controls. When compared to controls, very preterm IVF conceived infants were born to older women (mean ± SD of 32.4 ± 5.9 vs. 28.5 ± 6.4 years, p=0.01), but other demographic data (primigravida status, race, ethnicity, rural residence, receipt of antenatal corticosteroids) were similar.

Compared to controls, IVF conceived patients were less likely to have Respiratory Distress Syndrome and receive surfactant therapy (9 [33%] vs. 33 [61.1%], p=0.009). Other in-hospital outcomes (intraventricular hemorrhage, bronchopulmonary dysplasia, necrotizing enterocolitis, retinopathy of prematurity) were similar between the two cohorts. Neurodevelopmental data were also similar between cohorts at 5-6 months (15% of IVF at high risk for ND delay vs. 16.7% of controls, p=0.98), 12 months (9% vs. 4%, p=0.41) and 24 months (14% vs. 19%, p=0.32).

**Table 2: Analyses of BINS Neurodevelopmental Outcome Data**

	IVF Patients	Control Patients	All Patients	p-value
<b>BINS Score at five to six months corrected age</b>				
low risk	6 (30.0%)	11 (30.6%)	17 (30.4%)	0.982
moderate risk	11 (55.0%)	19 (51.4%)	30 (52.6%)	
high risk	3 (15.0%)	6 (16.2%)	9 (15.8%)	
<b>BINS Score at 12 months corrected age</b>				
low risk	9 (39.1%)	6 (25.0%)	15 (31.9%)	0.412
moderate risk	12 (52.2%)	17 (70.8%)	29 (61.7%)	
high risk	2 (8.7%)	1 (4.2%)	3 (6.4%)	
<b>BINS Score at 24 months corrected age</b>				
low risk	9 (64.3%)	6 (37.5%)	15 (50.0%)	0.320
moderate risk	3 (21.4%)	7 (43.8%)	10 (33.3%)	
high risk	2 (14.3%)	3 (18.8%)	5 (16.7%)	

## Discussion/Conclusions

- Infants born preterm after IVF conception have similar in-hospital and neurodevelopmental outcomes when compared to matched preterm infants
- This is reassuring information that can be shared with individuals considering IVF
- The reasons for a higher-than-expected incidence of preterm birth (33%) after conception via IVF are unclear and require further investigation
- Limitations include the retrospective nature of this study and patients lost to follow up