ASSOCIATION OF IVF WITH SEVERE NEONATAL MORBIDITY

Rachel Solmonovich, MD[a,b], Frank I. Jackson, DO[a, B], Alejandro Alvarez, MPH[a,c], Matthew J. Blitz, MD, MBA[a,b,d]

[a]Northwell, New Hyde Park, NY
[b]Department of Obstetrics and Gynecology, South Shore University Hospital, Bay Shore, NY; Zucker School of Medicine, Hempstead, NY
[c]Biostatistics Unit, Office of Academic Affairs, Northwell Health, New Hyde Park, NY.
[d]Institute of Health Systems Science, Feinstein Institutes for Medical Research, Northwell Health, Manhasset, NY.

Background: In vitro fertilization (IVF) is a common assisted reproductive technology linked to higher complications. A composite neonatal adverse outcome indicator that reliably identifies infants with significantly increased risk for hospital readmission or death in the first year of life has been validated in both Australia and the UK. While several studies have shown an increased risk of adverse neonatal outcomes in pregnancies conceived via IVF, none have evaluated this robust indicator of severe outcomes.

Objective: The primary objective was to determine the association between IVF and severe neonatal morbidity (SNM). A secondary objective was to assess whether IVF is associated with the administration of antenatal steroids for fetal lung maturity.

Material and Methods: A retrospective cohort study of all live singleton deliveries at ≥ 23 weeks gestational age at two tertiary hospitals in NY from 2019-2023. Patients with missing mode of conception data were excluded. The primary exposure was IVF. The primary outcome was SNM, a composite neonatal adverse outcome indicator which includes diagnoses and procedures, minimally modified from the validated composite neonatal outcome indicator (Table 1). The secondary outcome was steroid administration. Data collected from electronic medical records included maternal demographics, health insurance, parity, preferred language, mode of delivery, obstetric comorbidity index (OB-CMI) score, and obstetric and neonatal variables. The OB-CMI score is based on 24 weighted comorbidity indicators identified by ICD-10 codes and clinical documentation. It is a validated tool that predicts severe maternal morbidity. Inferential statistics were performed to determine if there was a significant difference in outcomes between cohorts. A p-value of <0.05 was considered statistically significant. Multivariable logistic regression analysis was used to model the probability of SNM as a function of IVF, while adjusting for covariate factors.

Results: A total of 47,433 patients were included for this study: 2,378 IVF pregnancies and 45,055 non-IVF pregnancies. The study population was predominantly Non-Hispanic White, English speaking, and multiparous. The SNM rate of patients who conceived via IVF was 12.45% (n=296), compared to 8.21% (n=3,700) among the non-IVF group (OR 1.59, 95% CI: 1.40-1.80). Adjusted ORs are shown in Table 2 and Figure 1. Steroid administration occurred more frequently in the IVF cohort (8.54% vs. 6.38%, p<0.0001).

Conclusions: Our results indicate that patients undergoing IVF are more likely to have newborns that experience SNM. The higher rates of antenatal steroid administration seen in the IVF cohort are likely due to their higher risk of preterm delivery. Rates of SNM would likely be even higher in this cohort without antenatal steroid administration. Future studies could review the specific mechanisms underlying this elevated SNM risk to optimize antenatal surveillance and counseling for IVF-conceived pregnancies and to aid healthcare providers and patients in making informed decisions.

Table 1: SNM variables

Variables	
Any body cavity surgery	Mechanical ventilation
Birthweight less than 1500 grams	Necrotizing enterocolitis
Blood transfusion	Neonatal resuscitation
Brachial plexus injury	Periventricular leukomalacia
Bronchopulmonary dysplasia	Pneumonia
Chest tube insertion	Pneumothorax
CPAP continuous positive airway pressure	Respiratory distress syndrome
Death within 28 days or before discharge	Retinopathy of prematurity
Exchange transfusion	Seizure
Gestational age less than 32 weeks	Sepsis
Hypoxic ischemic encephalopathy	Stroke
Intraventricular hemorrhage	

Table 2: Multivariable Logistic Regression Model

	SNM n=3,996	No SNM n=43,437	aOR Ratio (95% CI)
IVF			
Yes	296 (12.52)	2,082 (87.55)	1.41 (1.24-1.61)
No	3,700 (8.21)	41,355 (91.79)	1 (reference)
Race/ethnicity			
Asian or Pacific Islander	644 (7.29)	8,195 (92.71)	1.07 (0.97-1.18)
Hispanic	641 (9.99)	5,774 (90.01)	1.30 (1.17-1.44)
Non-Hispanic Black	915 (12.20)	6,587 (87.80)	1.46 (1.33-1.60)
Non-Hispanic White	1,304 (6.83)	17,793 (93.17)	1 (reference)
Other or multiracial	353 (8.45)	3,825 (91.55)	1.16 (1.02-1.31)
Declined or unknown	139 (9.91)	1,263 (90.09)	1.45)1.20-1.74)
Public Health Insurance			
Yes	1,443 (10.44)	12,381 (89.56)	1.32 (1.23-1.42)
No	2,553 (7.60)	31,056 (92.40)	1 (reference)
OB-CMI score			
0	1,011 (5.49)	17,403 (94.51)	1 (reference)
1	626 (6.23)	9,426 (93.77)	1.14 (1.03-1.27)
2	571 (7.96)	6,604 (92.04)	1.44 (1.29-1.60)
3	368 (9.21)	3,626 (90.79)	1.65 (1.45-1.87)
≥4	1,420 (18.21)	6,378 (81.79)	3.51 (3.22-3.84)

Figure 1:

Odds of Severe Neonatal Morbidity
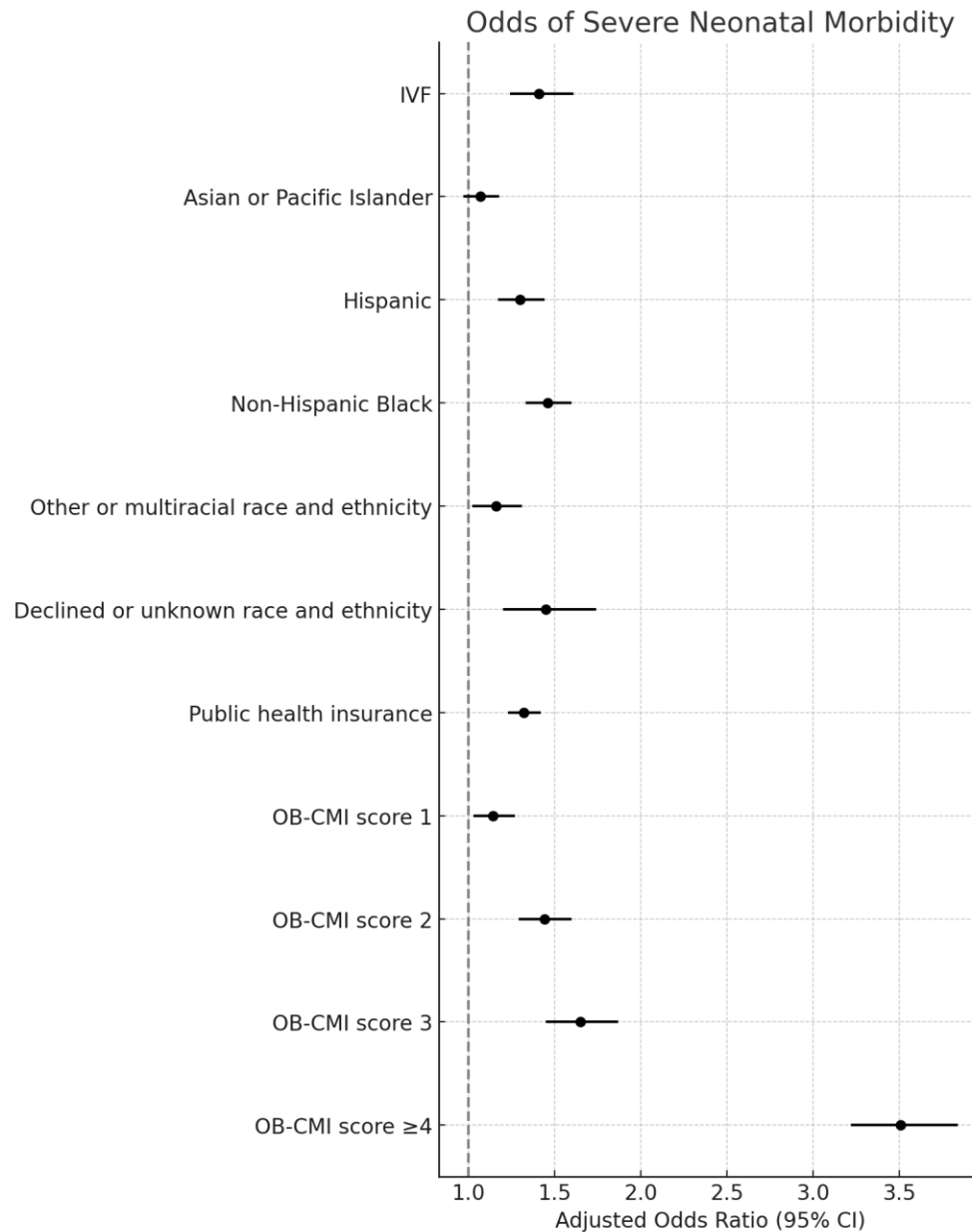
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