Advanced Paternal Age and Placental-Mediated Perinatal Outcomes in U.S. Singleton Births: Threshold Effects and Racial/Ethnic Heterogeneity

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ABSTRACT

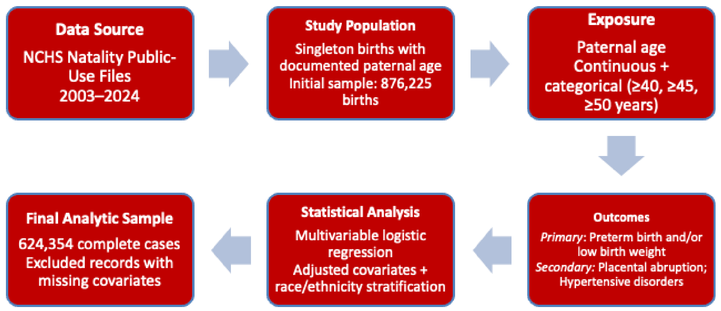
Context: Advanced paternal age (APA) has been associated with adverse reproductive outcomes, but its relationship with placental-mediated pregnancy outcomes remains unclear. We evaluated whether APA is associated with placental-mediated adverse perinatal outcomes and whether this association varies across population subgroups.
Methods: We conducted a retrospective cohort study of 876,225 singleton births using the National Center for Health Statistics Natality Public-Use Files (2003–2024). Paternal age was analyzed continuously and categorically (≥40, ≥45, and ≥50 years). Multivariable logistic regression assessed associations with a composite placental-mediated outcome (preterm birth and/or low birth weight), adjusting for maternal and pregnancy-related covariates.
Results: Advanced paternal age was associated with increased odds of the composite outcome, with risk rising at older paternal age thresholds. The association differed by race/ethnicity, persisting among Non-Hispanic White, Hispanic, and Asian mothers but not among Non-Hispanic Black or American Indian/Alaska Native mothers.
Conclusion: Advanced paternal age was independently associated with placental-mediated adverse pregnancy outcomes, although the magnitude of risk varied across racial and ethnic groups, supporting individualized reproductive risk assessment.

INTRODUCTION

The placenta functions as a dynamic structure that connects the mother and fetus, facilitating fetal growth and nutrient exchange. Factors present prior to conception not only influence placental development but may also affect subsequent obstetric outcomes[1]. Evidence suggests that paternally expressed genes play an important role in placental development and function[2]. Despite this, the literature has largely focused on maternal factors affecting obstetric outcomes, with comparatively less attention given to paternal factors, particularly paternal age.

This gap is increasingly relevant as parenthood is being delayed in many developed countries, including the United States. The mean paternal age in the United States increased from 27.4 years in 1972 to 30.9 years in 2015 (Figure 1), while the proportion of births to fathers older than 40 years doubled during the same period[3]. As men age, age-related changes in sperm have been associated with adverse reproductive outcomes, including preterm birth, low birth weight, and low Apgar scores[3]. However, the independent contribution of advanced paternal age (APA) to placental-mediated perinatal outcomes remains incompletely understood.

METHODS



RESULTS

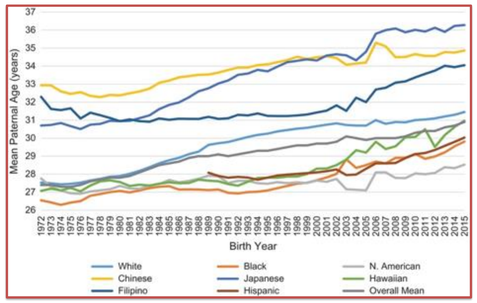


Figure 1: Temporal trend of mean paternal age by race from 1972 to 2015.[4]

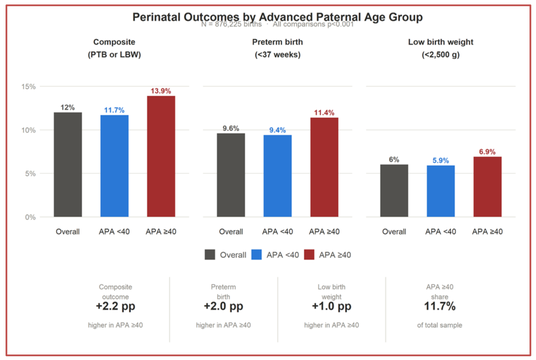


Figure 2: Percentage of composite placental-mediated adverse perinatal outcomes overall and by paternal age group (<40 vs. ≥40 years)

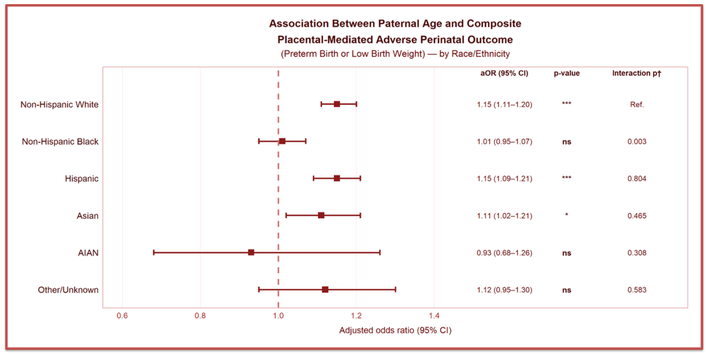


Figure 3: Adjusted odds ratios (95% CI) for the association between advanced paternal age (≥40 years) and the composite placental-mediated adverse perinatal outcome by race/ethnicity

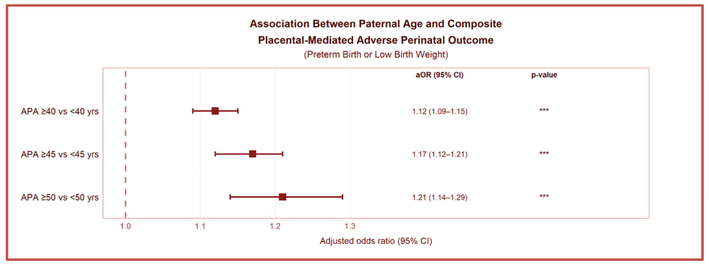


Figure 4: Adjusted odds ratios (95% CI) for the association between advanced paternal age (≥40 years) and preterm birth and low birth weight

DISCUSSION

- Advanced paternal age (APA) was associated with a higher prevalence of composite placental-mediated adverse outcomes (Figure 2).
- The association between paternal age and outcomes were not linear; continuous models were null after adjustment, suggesting no incremental year-by-year risk once confounders were accounted for.
- In contrast, categorical analyses demonstrated a threshold and dose-dependent effect, with increased risk beginning at approximately ≥40 years and progressively higher odds at ≥45 and ≥50 years (Figure 4).
- The association varied across racial and ethnic groups, suggesting potential modification by social, environmental, or structural factors that warrant further investigation (Figure 3).
  - Associations were present among Non-Hispanic White, Hispanic, and Asian groups
  - No significant association was observed among Non-Hispanic Black or American Indian/Alaska Native groups
- Overall, findings support a model in which APA (≥40 years) is a modest but consistent risk marker for placental-mediated outcomes, independent of maternal age and hypertensive disease, but primarily evident in non-linear, threshold-based analyses.

CONCLUSIONS

- Advanced paternal age is associated with increased odds of placental-mediated adverse pregnancy outcomes.
- Risk becomes apparent at paternal age 40 and increases with older age thresholds.
- The association is not uniform across racial and ethnic groups, indicating heterogeneity in risk.
- These findings support considering paternal age in a more individualized framework for reproductive risk assessment.

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