



Are women of advanced maternal age at increased risk for severe maternal morbidity?

Yes. Severe maternal morbidities, including renal failure, shock, amniotic fluid embolism, and cardiac morbidity, **were significantly increased for women older than 39 years**, according to results of a study that included more than 800,000 singleton births over 10 years. The observed increases in maternal morbidity persisted after controlling for assisted conception and comorbid medical conditions.

Lisonkova S, Potts J, Muraca GM, et al. Maternal age and severe maternal morbidity: a population-based retrospective cohort study. PLoS Med. 2017;14(5):e1002307.

► EXPERT COMMENTARY

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While numerous studies have investigated the risk of perinatal outcomes with advancing maternal age, the primary objective of a recent study by Lisonkova and colleagues was to examine the association between advancing maternal age and severe maternal morbidities and mortality.

Details of the study

The population-based retrospective cohort study compared age-specific rates of severe maternal morbidities and mortality among 828,269 pregnancies in Washington state between 2003 and 2013. Singleton births to

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women 15 to 60 years of age were included; out-of-hospital births were excluded. Information was obtained by linking the Birth Events Record Database (which includes information on maternal, pregnancy, and labor and delivery characteristics and birth outcomes), and the Comprehensive Hospital Abstract Reporting System database (which includes diagnostic and procedural codes for all hospitalizations in Washington state).

The primary objective was to examine the association between age and severe maternal morbidities. Maternal morbidities were divided into categories: antepartum hemorrhage, respiratory morbidity, thromboembolism, cerebrovascular morbidity, acute cardiac morbidity, severe postpartum hemorrhage, maternal sepsis, renal failure, obstetric shock, complications of anesthesia and obstetric interventions, and need for life-saving procedures. A composite outcome, comprised of severe maternal morbidities, intensive care unit admission, and maternal mortality, was also created.

Rates of severe morbidities were compared for age groups 15 to 19, 20 to 24, 25 to 29, 30 to 34, 35 to 39, 40 to 44, and ≥ 45 years to the referent category (25 to 29 years). Additional comparisons were also performed for

FAST TRACK

The primary study objective, in 828,269 pregnancies in women aged 15 to 60 years, was to examine the association between age and severe maternal morbidities

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ages 45 to 49 and ≥ 50 years for the composite and for morbidities with high incidence. Logistic regression and sensitivity analyses were used to control for demographic and prepregnancy characteristics, underlying medical conditions, assisted conception, and delivery characteristics.

Severe maternal morbidities demonstrated a J-shaped association with age: the lowest rates of morbidity were observed in women 20 to 34 years of age, and steeply increasing rates of morbidity were observed for women aged 40 and older. One notable exception was the rate of sepsis, which was increased in teen mothers compared with all other groups.

The unadjusted rate of the composite outcome of severe maternal morbidity and mortality was 2.1% in teenagers, 1.5% among women 25 to 29 years, 2.3% among those aged 40 to 44, and 3.6% among women aged 45 and older.

Although rates were somewhat attenuated after adjustment for demographic and prepregnancy characteristics, chronic medical conditions, assisted conception, and delivery characteristics, most morbidities remained significantly increased among women aged 39 years and older, including the composite outcome. Among the individual morbidities considered, increased risk was highest for renal failure, amniotic fluid embolism, cardiac morbidity, and shock, with adjusted odds ratios of 2.0 or greater for women older than 39 years.

Study strengths and weaknesses

This study contributes substantially to the existing literature that demonstrates higher rates of pregnancy-associated morbidities in women of increasing maternal age.^{1,2} Prior studies in this area focused on perinatal morbidity and mortality and on obstetric

WHAT THIS EVIDENCE MEANS FOR PRACTICE

This large, retrospective study (level II evidence) suggests that women of advancing age are at significantly increased risk of severe maternal morbidities, even after controlling for preexisting medical conditions. We therefore recommend that clinicians inform and counsel women who are considering pregnancy at an advanced age, and those considering oocyte cryopreservation as a means of extending their reproductive life span, about the increased maternal morbidities associated with pregnancy at age 40 and older.

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outcomes such as cesarean delivery.³⁻⁵ This large-scale study examined the association between advancing maternal age and a variety of serious *maternal* morbidities. In another study, Callaghan and Berg found a similar pattern among mortalities, with high rates of mortality attributable to hemorrhage, embolism, and cardiomyopathy in women aged 40 years and older.¹

Exclusion of multiple gestations. As in any study, we must consider the methodology, and it is notable that Lisonkova and colleagues' study excluded multiple gestations. Given the association with advanced maternal age, assisted reproductive technology, and the incidence of multiple gestations, a high rate of multiple gestations would be expected among women of advanced maternal age. (Generally, maternal age of at least 35 years is considered "advanced," with greater than 40 years "very advanced.") Since multiple gestations tend to be associated with increases in morbidity, excluding these pregnancies would likely bias the study results toward the null. If multiple gestations had been included, the rates of serious maternal morbidities in older women might be even higher than those demonstrated, potentially strengthening the associations reported here. ☹



Severe maternal morbidities showed a J-shaped association with age. The lowest morbidity rates were seen in 20- to 34-year-olds, with steeply rising morbidity rates observed in women aged 40 and older.

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