

Studies identify most common causes, risk factors for stillbirth

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Common causes for stillbirth include obstetric complications and placental abnormalities, while factors that could be known at the start of pregnancy, such as previous stillbirth or pregnancy loss, were associated with an increased risk for stillbirth, although these and other factors accounted for only a small proportion of the overall risk, according to two studies in the December 14 issue of *JAMA*.

"Stillbirth, defined as fetal death at 20 weeks' gestation or later, is one of the most common adverse pregnancy outcomes in the United States and affects approximately 1 in 160 pregnancies. These approximately 26,000 stillbirths per year are equivalent to the number of infant deaths. The stillbirth rate in the United States is higher than that of many other developed countries," according to background information in the first article. "Since 2003 the stillbirth rate in the United States has remained stagnant at 6.2 stillbirths per 1,000 births, 59 percent higher than the Healthy People 2010 target goal of 4.1 fetal deaths per 1,000 births."

Robert M. Silver, M.D., of the University of Utah School of Medicine, Salt Lake City, and colleagues with the Stillbirth Collaborative Research Network Writing Group, conducted a study to determine the causes of stillbirth in a racially and geographically diverse population in the United States. The study was conducted from March 2006 to September 2008 with surveillance for all stillbirths at 20 weeks or later in 59 tertiary care and community hospitals in 5 areas defined by state and county boundaries to ensure access to at least 90 percent of all deliveries. Standardized evaluations were performed at delivery.

Of 663 women with stillbirth enrolled, 500 women consented to complete postmortem examinations of 512 neonates. A probable cause of death was found in 312 of the stillbirths (60.9 percent) and a possible or probable cause in 390 cases (76.2 percent). There was more than 1 probable or possible cause of death in 161 stillbirths (31.4 percent). The researchers found that obstetric complications were the most common category for cause of death (150 cases [29.3 percent]); placental abnormalities were indicated in 121 cases (23.6 percent). "Other causes included fetal genetic/structural abnormalities in 70 cases (13.7 percent), infection in 66 (12.9 percent), umbilical cord abnormalities in 53 (10.4 percent), hypertensive disorders in 47 (9.2 percent), and maternal medical complications in 40 (7.8 percent)," the authors write.

The researchers also found that non-Hispanic black women experienced a higher proportion of stillbirths associated with obstetric complications compared with non-Hispanic white women and Hispanic women combined (43.5 percent [50] vs. 23.7 percent [85]); and infections (25.2 percent [29] vs. 7.8 percent [28]). Cord abnormalities were associated with a higher proportion of stillbirths in non-Hispanic white and Hispanic women compared with non-Hispanic black and other women.

The authors note that the sources most likely to provide positive information regarding cause of death were placental histology, perinatal postmortem examination, and karyotype (an evaluation of the chromosomes).

"The U.S. stillbirth rate has remained unacceptably high, affecting 1 in 160 pregnancies each year. Reduction in the stillbirth rate will require thorough investigation into the cause of death. After a systematic and thorough evaluation, a cause of death was determined in the majority of cases of stillbirth in our study. Therefore, postmortem examination, placental histology, and karyotype are strongly recommended as part of the diagnostic evaluation. In addition, the development of interventions

to prevent stillbirth should consider the observed differential distribution of causes of death as gestational age advances, as well as variation by race/ethnicity," the researchers conclude.

Various Risk Factors Known At Time of Pregnancy May Help Gauge Risk of Stillbirth

In another study in the December 14 JAMA, George R. Saade, M.D., of the University of Texas Medical Branch at Galveston, and colleagues with the Stillbirth Collaborative Research Network Writing Group, examined the relation between stillbirths and risk factors that could be ascertained at the start of pregnancy, particularly the contribution of these factors to the racial disparities that exist with stillbirths.

"Many of the factors associated with stillbirth need to be addressed early in pregnancy. Although other factors may be important later in pregnancy, clinicians providing obstetrical care frequently spend relatively more time at the initial visits counseling patients regarding their risk of adverse pregnancy outcomes," the authors write.

The multisite population-based case-control study was conducted between March 2006 and September 2008 at 59 U.S. tertiary care and community hospitals, with access to at least 90 percent of deliveries within 5 areas defined by state and county lines. The study enrolled residents with deliveries of 1 or more stillborn fetuses and a representative sample of deliveries of only live-born infants, which was supplemented by oversampling of women delivering at less than 32 weeks' gestation and those of African descent delivering at 32 weeks' gestation or greater. The analysis included 614 case and 1,816 control deliveries.

The researchers found that after analyses, a number of maternal factors

were independently associated with stillbirth: non-Hispanic black race/ethnicity; diabetes; age 40 years or older; AB blood type; history of drug use with addiction; history of cigarette smoking during the 3 months prior to pregnancy; being overweight or obese; and not living with a partner.

Several reproductive history factors were strongly associated with stillbirth, including previous stillbirth and nulliparity (a woman who has never borne a child) with and without a history of prior spontaneous losses at less than 20 weeks' gestation and plural (multiple, i.e., twins) birth in the current pregnancy.

The authors note that overall, pregnancy factors known at the start of pregnancy accounted for little of the stillbirth risk. Apart from occurrence of previous stillbirth or pregnancy loss, the other risk factors have limited predictive value, they write.

"Further research is needed to identify pregnancies at highest risk overall and for specific causes. Although some of the risk factors may not be modifiable (e.g., race/ethnicity), knowledge of interactions between these factors and other modifiable ones may be useful. In addition, association studies aid in the identification of areas of investigation and preventive approaches. For example, non-Hispanic black women have a more than 2-fold increase in risk of stillbirth. However, the disparity in risk largely occurs at less than 24 weeks' gestation. Therefore, focusing on the pathophysiology of early preterm birth may reduce racial disparity in stillbirth," the researchers conclude.

Jay D. Iams, M.D., and Courtney D. Lynch, Ph.D., M.P.H., of The Ohio State University Medical Center, Columbus, comment on the findings of these studies in an accompanying editorial.

"The Stillbirth Collaborative Research Network (SCRN) reports add to

the increasing realization that the current obstetrical taxonomy [classifications] is an obstacle to improving pregnancy outcomes. Optimal investigation of the origins, treatment, and prevention of stillbirth and preterm birth will require data collected on deliveries before and after 20 weeks, regardless of whether the fetus is alive or not at the time of presentation for care."

"As the SCRN work highlights, pregnancies involving fetal death near the limit of viability, including those before 20 weeks, share important commonalities with pregnancies resulting in early preterm birth. As such, the reports from the SCRN will not only further the understanding of stillbirth but should also encourage the need to reframe thinking about how to address the problem of spontaneous preterm birth and the associated racial/ethnic disparities."

More information: *JAMA*. 2011;306[22]:2459-2468.
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