OBSTETRICS

The risk of stillbirth and infant death by each additional week of expectant management in twin pregnancies

Jessica M. Page, MD; Rachel A. Pilliod, MD; Jonathan M. Snowden, PhD; Aaron B. Caughey, MD, PhD

OBJECTIVE: The objective of the study was to compare the fetal/infant mortality risk associated with each additional week of expectant management with the mortality risk of immediate delivery in women with twin gestations.

STUDY DESIGN: A retrospective cohort study was performed utilizing 2006–2008 National linked birth certificate and death certificate data. The incidence of stillbirth and infant death were determined for each week of pregnancy from 32 0/7 weeks' through 40 6/7 weeks' gestation. Pregnancies complicated by fetal anomalies were excluded. These measures were combined to estimate the theoretic risk of remaining pregnant an additional week by adding the risk of stillbirth during the extra week of pregnancy with the risk of infant death encountered with delivery during the following week. This composite fetal/infant mortality risk was compared with the risk of infant death associated with delivery at the corresponding gestational age.

RESULTS: The risk of stillbirth increased with increasing gestational age, for example, between 37 and 38 weeks' gestation (12.5 per 10,000 vs 22.5 per 10,000; $P < .05$). As expected, the risk of infant death following delivery gradually decreased as pregnancies approached term gestation. Week-by-week differences were statistically significant ($P < .05$) between 32 and 36 weeks with decreasing risk of infant death at advancing gestational ages. The composite risk of stillbirth and infant death associated with an additional week of pregnancy had a significant increase from 37 to 38 weeks' gestation (43.9 per 10,000 vs 59.2 per 10,000; $P < .05$). At 37 weeks' gestation, the relative risk of mortality was statistically significantly lower with immediate delivery as compared with expectant management (relative risk, 0.87; 95% confidence interval, 0.77–0.99).

CONCLUSION: Our results suggest that fetal/infant death risk is minimized at 37 weeks' gestation; however, individual maternal and fetal characteristics must also be taken into account when determining the optimal timing of delivery for twin pregnancies.

Key words: expectant management, infant death, stillbirth, twin pregnancy

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Twin pregnancies are at an increased risk of stillbirth, antenatal morbidity, and infant death compared with singleton gestations.[1] This is largely due to uteroplacental insufficiency, preterm delivery, and maternal antenatal complications. Maternal comorbidities such as advanced maternal age, gestational diabetes, and hypertensive disorders are also more common in twin gestations and impart an elevated stillbirth risk.[2,3]

The risk of stillbirth has also been shown to vary with gestational age at delivery in twin pregnancies with an increasing risk at later gestational ages.[4-6] There has been considerable debate regarding the contribution of chorionicity to stillbirth risk in uncomplicated twin gestations. Several studies have concluded that even in the absence of monochorionic-specific risks such as twin-twin transfusion syndrome, monochorionic pregnancies experience an increased rate of stillbirth.[7,8] Subsequent work has not demonstrated this phenomenon, finding more equivalent risks of stillbirth in monochorionic and dichorionic pregnancies during the late preterm period.[4,9-13]

Infant death rates are 5 times higher overall following twin gestations as compared with singleton pregnancies. Complications of prematurity, congenital

From the Department of Obstetrics and Gynecology, University of Utah School of Medicine, Salt Lake City, UT (Dr Page); Department of Obstetrics and Gynecology, Brigham and Womens Hospital and Massachusetts General Hospital, Boston, MA (Dr Pilliod); and Department of Obstetrics and Gynecology, Oregon Health and Science University, Portland, OR (Drs Snowden and Caughey).

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Corresponding author: Jessica Page, MD. jessica.page@hsc.utah.edu

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anomalies, and low birthweight are the primary risk factors for infant mortality in these cases.[1] The risk of infant death varies by gestational age at delivery. Infant death risk is highest in preterm deliveries with decreasing incidence as pregnancy approaches term gestation. The primary causes of death in these cases have been shown to be sudden infant death syndrome, asphyxia, and sepsis.[14-18]

The increased risk of both stillbirth and complications of iatrogenic prematurity create a challenging situation when determining the appropriate gestational age for delivery, requiring careful consideration of tradeoffs. Prior research has suggested that for uncomplicated monochorionic and dichorionic pregnancies, delivery between 36 and 38 weeks' gestational age minimizes fetal and infant mortality.[4-6,9,13] Additionally, a recent Cochrane review concluded that for uncomplicated twin pregnancies elective delivery at 37 weeks did not impart an increased risk of neonatal/infant complications.[19] However, the known complications of late preterm and early term delivery including respiratory distress syndrome and neonatal intensive care unit (NICU) admission must be taken into account when determining the appropriate gestational age for delivery.[20-28]

Given this delicate balance of stillbirth risk and complications of iatrogenic prematurity, the decision regarding delivery timing for otherwise uncomplicated twin pregnancies is challenging. Using a previously devised composite measure, we sought to determine the risk of stillbirth and infant death by week of gestation in twin pregnancies and to quantify the risk of expectant management vs delivery during the late third trimester.

Materials and Methods

A retrospective cohort study was conducted utilizing 2006-2008 national linked birth certificate and death certificate data. The National Center for Health Statistics links live birth cohort data with infant and fetal death information.[1]

We utilized stillbirth data at each gestational age week and infant death data following live births at each gestational age week. Data were investigated for twin pregnancies from 20 weeks' through 42 weeks' gestational age. Comparisons were made by the individual fetus or infant as opposed to the pair present in each pregnancy. Exclusion criteria included pregnancies complicated by fetal anomalies.

Additional characteristics of our study population were also determined including gestational diabetes, hypertensive disorders, and intrauterine growth retardation (IUGR). To eliminate the potential confounding effect these factors may have on our results we conducted a secondary analysis excluding gestational diabetes, hypertensive disorders and IUGR. To better characterize the morbidity associated with late preterm and early term deliveries, neonatal outcomes by gestational age including NICU admission, neonatal seizures, and a need for ventilation for greater than 6 hours were determined.

Our study population included fetal deaths and live births following delivery from 32 0/7 through 40 6/7 weeks' gestational age. Pregnancy dating was determined using the best obstetric estimate. This most often refers to the last menstrual period with an allowance of the correction of gestational age if the estimated age based on the last menstrual period is significantly different from that estimated by ultrasound.[29] Stillbirth was designated as fetal death following 20 weeks' gestational age. Infant death was designated as death occurring within the first year of life.

This study was approved by the Institutional Review Board at Oregon Health and Science University.

Stillbirth risk was determined using a fetuses at-risk life table method. This method accounts for all ongoing fetuses in the denominator with exclusion of half the deliveries occurring during the gestational age week. This technique is used to reflect the fact that a portion of pregnancies will have delivered at any given time during the gestational age week being studied and stillbirths occur in an even distribution throughout the week of gestation.[30] The calculation includes the number of stillbirths occurring at a given gestational age in the numerator divided by the fetuses at-risk as described above (Figure 1, equation 1).

Infant death risk was calculated by dividing the number of infant deaths by the number of live births at the corresponding gestational age (Figure 1, equation 2). To estimate the risk of fetal/infant mortality associated with each additional week of pregnancy, a composite risk was calculated. This calculation included the risk of stillbirth associated with the additional week of pregnancy in addition to the risk of infant death following the gestational age at delivery (Figure 1, equation 3).

Stillbirth, infant death, and composite fetal/infant mortality risks were determined for each week of gestation in twin pregnancies from 32 0/7 through 40 6/7 weeks' gestational age. This period was chosen because of the prevalence of preterm and early term delivery in this population with rare occurrence of delivery past 40 weeks' gestation. Stata software (version 11; Stata Corp, College

FIGURE 1
Stillbirth, infant death, and expectant management risk calculations

Equation 1. $$\frac{\text{N stillbirths}_{GA}}{(\text{N fetuses}_{GA} - 0.5*\text{N deliveries}_{GA})}$$

Equation 2. $$\frac{\text{N infant deaths}_{GA}}{\text{N deliveries}_{GA}}$$

Equation 3. $$\text{Equation 1}_{GA\,x} + \text{Equation 2}_{GA\,x+1}$$

Equation 1 describes the stillbirth risk calculation, which takes into account fetuses at risk by dividing the number of stillbirths by all ongoing fetuses minus half the deliveries occurring at the gestational age week studied. Equation 2 displays the infant death calculation with the number of infant deaths divided by the total number of live births at that gestational age. Equation 3 shows the composite risk associated with expectant management with the stillbirth risk during the additional week of expectant management added to the infant death risk following delivery at the subsequent week.

GA, gestational age.

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