What is the optimal time for delivery in women with gestational hypertension?

Meredith O. Cruz, MD, MPH/MBA; Weihua Gao, MS; Judith U. Hibbard, MD

OBJECTIVE: To assess the optimal timing of delivery for women with gestational hypertension.

STUDY DESIGN: A multicenter database that contained 228,668 deliveries was used to extract data on gravids with gestational hypertension. The week-specific rates of maternal and neonatal morbidity/mortality were calculated after induction of labor. Point wise 95% confidence intervals were calculated around each of these gestational age-specific rates.

RESULTS: After induction of labor, the rate of maternal morbidity/mortality reached a nadir of 89.9 per 1000 live births (95% confidence interval, 68.1–111.8) at 38-39 6/7 weeks’ gestation, although the rate of neonatal morbidity/mortality fell to 10.5 per 1000 live births (95% confidence interval, 2.8–18.2) at 39-39 6/7 weeks. There were only 3 total stillbirths in our study cohort.

CONCLUSION: In women with gestational hypertension, induction of labor between 38- and 39-weeks’ balances the lowest maternal and neonatal morbidity/mortality.

Keywords: delivery, gestational hypertension, maternal and neonatal outcomes

Hypertension is one of the most common medical disorders in pregnancy and a major cause of maternal and perinatal morbidity and death. Approximately 70% of women diagnosed with hypertension during pregnancy will have gestational hypertension or preeclampsia, which complicates 6% to 8% of all pregnancies. Women with gestational hypertension progress to mild preeclampsia and severe preeclampsia at rates of 46% and 9.6%, respectively.

The majority of gestational hypertension and mild preeclamptic cases occur after 36-weeks’ gestation, but there is conflicting evidence and controversy regarding the timing for delivery of these women. The decision to induce labor at a given gestational age involves weighing the maternal and fetal risks associated with allowing a pregnancy to continue against the risks after delivery. It was previously thought that women with mild hypertensive disease occurring at 37-weeks’ gestation or later have a pregnancy outcome similar to that found in normotensive women, and previous recommendations have included outpatient management in those who were compliant, with induction of labor near term.

However, as recently demonstrated, gravidas with mild disease (gestational hypertension or mild preeclampsia) allocated to expectant monitoring developed adverse maternal outcomes in 44% compared with 31% assigned to induction of labor (relative risk [RR], 0.71; 95% confidence interval [CI], 0.59–0.86; P < .0001). Thus, induction of labor has now been suggested for women with mild hypertensive disease who have achieved 37-weeks’ gestation. However, Koopmans et al did not separate those with gestational hypertension from women with mild preeclampsia, making it unclear whether morbidities were similar and recommendations should be the same for both. Although early delivery of the fetus may prevent stillbirth and other morbidities associated with ongoing pregnancy, recent evidence from general obstetric populations suggests that there are increased risks of serious neonatal morbidity (eg, prolonged hospitalization, sepsis, adverse respiratory outcomes) associated with delivery at 36, 37, and 38 weeks of gestation compared with 39 or 40 weeks.

The objective of this study was to assess the optimal timing of delivery for women with gestational hypertension by quantifying the risks of adverse maternal and fetal outcomes associated with induction of labor at each gestational week, from 36 to 41 completed weeks, compared with those with ongoing pregnancy. We hypothesized that these risks would decrease at each advancing gestational week at or near term but would increase postterm.

MATERIALS AND METHODS

This is a retrospective cohort study from the Consortium on Safe Labor (CSL), which was sponsored by the Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD). The primary goal was to establish a comprehensive database from electronic medical records from...
multisite to characterize labor and delivery in a contemporary group of women experiencing current obstetric clinical practices. More detailed information regarding the CSL has been published. The electronic database contained 228,668 deliveries greater than 23 weeks from 12 clinical centers and 19 hospitals representing 9 American College of Obstetricians and Gynecologists districts between 2002 and 2008, with the majority (87%) of births occurring from 2005 through 2007 (reflecting the period when individual institutions initiated their electronic medical record systems). An inhouse obstetrician was available 24 hours per day at 11 of the 12 participating sites. Participating institutions provided data on maternal demographics, medical history, reproductive and prenatal history, labor and delivery information, postpartum, and newborn information. Data inquiries, cleaning, and logic checking were performed on the database. Validation studies were also performed to ensure that the electronic database was a reasonably accurate representation of the medical charts and was noted to be highly consistent (97.3-99.7%). Institutional Review Board approval was obtained by all participating institutions.

For the cohort of interest, we only included the first pregnancy, within the timeframe of data collection, from each subject in the database to avoid intraperson correlation, and excluded multiples, leaving 206,969 deliveries. We included all gravidas who met the definition for gestational hypertension or gestational age weeks. Gestational hypertension was defined as an elevation in blood pressure (BP) $\geq 140$ mm Hg systolic or $\geq 90$ mm Hg diastolic without proteinuria that developed in a woman after 20 weeks of gestation. All participating centers and investigators used standard criteria to define gestational hypertension; absence of proteinuria was diagnosed by urine dip, protein/creatinine ratio, or 24-hour urine collections according to local institutional standards. Pregnancies complicated by diabetes mellitus, cardiac, pulmonary, or renal disease were excluded. We calculated the stillbirth rates based on this entire cohort of women with gestational hypertension. Gravidas presenting for induction of labor were then extracted from this cohort for calculation of small for gestational age (SGA), stillbirth, and week-specific morbidity and mortality rates.

Maternal outcomes included serious morbidity, which was a composite defined as any of the following: intensive care unit (ICU) admission, abruption, large blood loss ($>0.5$ L SVD, $>1.0$ L

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**TABLE 1**

<table>
<thead>
<tr>
<th>Maternal characteristics</th>
<th>GHTN, n = 3588</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maternal age</td>
<td>Mean (± SD)</td>
</tr>
<tr>
<td>Age, y</td>
<td>26.6 (± 5.9)</td>
</tr>
<tr>
<td>Race, n (%)</td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>2218 (61.8)</td>
</tr>
<tr>
<td>Black/non-Hispanic</td>
<td>686 (19.1)</td>
</tr>
<tr>
<td>Hispanic</td>
<td>484 (13.5)</td>
</tr>
<tr>
<td>Asian/Pacific Islander</td>
<td>57 (1.6)</td>
</tr>
<tr>
<td>Other</td>
<td>143 (4.0)</td>
</tr>
<tr>
<td>Parity (mean), n (%)</td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>2128 (59.3)</td>
</tr>
<tr>
<td>1</td>
<td>746 (20.8)</td>
</tr>
<tr>
<td>2</td>
<td>408 (11.4)</td>
</tr>
<tr>
<td>3</td>
<td>178 (5.0)</td>
</tr>
<tr>
<td>≥4</td>
<td>128 (3.6)</td>
</tr>
<tr>
<td>BMI, mean (± SD)</td>
<td></td>
</tr>
<tr>
<td>Prepregnancy BMI, kg/m²</td>
<td>28.2 (± 7.1)</td>
</tr>
<tr>
<td>Delivery BMI, kg/m²</td>
<td>34.1 (± 6.9)</td>
</tr>
<tr>
<td>Blood pressure, mm Hg, mean (± SD)</td>
<td></td>
</tr>
<tr>
<td>Admit systolic BP</td>
<td>140.3 (± 13.4)</td>
</tr>
<tr>
<td>Admit diastolic BP</td>
<td>86.1 (± 11.7)</td>
</tr>
<tr>
<td>Admit mean arterial BP</td>
<td>104.2 (± 11.1)</td>
</tr>
<tr>
<td>Gestational age at delivery, wks</td>
<td>Mean (± SD)</td>
</tr>
<tr>
<td>Overall</td>
<td>38.5 (± 1.3)</td>
</tr>
<tr>
<td>Insurance, n (%)</td>
<td></td>
</tr>
<tr>
<td>Private</td>
<td>2210 (61.6)</td>
</tr>
<tr>
<td>Public</td>
<td>1207 (33.6)</td>
</tr>
<tr>
<td>Self-pay/unknown</td>
<td>171 (4.8)</td>
</tr>
<tr>
<td>Substance use, n (%)</td>
<td></td>
</tr>
<tr>
<td>Smoking</td>
<td>161 (4.5)</td>
</tr>
<tr>
<td>Alcohol</td>
<td>90 (2.5)</td>
</tr>
<tr>
<td>Illicit drug use</td>
<td>36 (1.1)</td>
</tr>
<tr>
<td>IUGR, n (%)</td>
<td></td>
</tr>
<tr>
<td>&lt;3rd percentile</td>
<td>74 (2.1)</td>
</tr>
<tr>
<td>&lt;10th percentile</td>
<td>258 (7.2)</td>
</tr>
</tbody>
</table>

BMI, body mass index; BP, blood pressure; GHTN, gestational hypertension; IUGR, intrauterine growth restriction.

Numbers and rates of stillbirth and serious maternal and neonatal morbidity/mortality among women with gestational hypertension

<table>
<thead>
<tr>
<th>GA, wks</th>
<th>Ongoing pregnancies, n</th>
<th>Stillbirth, n</th>
<th>Rate of stillbirth (per 1000 ongoing pregnancies)</th>
<th>Following induction of labor</th>
<th>Rate of maternal morbidity/mortality (per 1000 live births) [95% CI]</th>
<th>Live births, n</th>
<th>Neonatal deaths, n</th>
<th>Rate of maternal morbidity/mortality (per 1000 live births) [95% CI]</th>
</tr>
</thead>
<tbody>
<tr>
<td>36</td>
<td>3588</td>
<td>0</td>
<td>—</td>
<td>24</td>
<td>106.2 [66.0–146.4]</td>
<td>226</td>
<td>1</td>
<td>24</td>
</tr>
<tr>
<td>37</td>
<td>3208</td>
<td>2</td>
<td>0.6</td>
<td>53</td>
<td>121.8 [91.1–152.6]</td>
<td>435</td>
<td>0</td>
<td>13</td>
</tr>
<tr>
<td>38</td>
<td>2521</td>
<td>1</td>
<td>0.4</td>
<td>59</td>
<td>89.9 [68.1–111.8]</td>
<td>656</td>
<td>0</td>
<td>12</td>
</tr>
<tr>
<td>39</td>
<td>1527</td>
<td>0</td>
<td>—</td>
<td>69</td>
<td>103.0 [80.0–126.0]</td>
<td>670</td>
<td>0</td>
<td>7</td>
</tr>
<tr>
<td>40</td>
<td>595</td>
<td>0</td>
<td>—</td>
<td>37</td>
<td>103.9 [72.2–135.6]</td>
<td>356</td>
<td>0</td>
<td>10</td>
</tr>
<tr>
<td>41</td>
<td>89</td>
<td>0</td>
<td>—</td>
<td>7</td>
<td>129.6 [40.0–219.2]</td>
<td>54</td>
<td>2</td>
<td>37.0 [–13.3 to 87.4]</td>
</tr>
<tr>
<td>≥42</td>
<td>7</td>
<td>0</td>
<td>—</td>
<td>0</td>
<td>0</td>
<td>4</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

CI, confidence interval; GA, gestational age.

* GA defined as completed weeks (ie, 36 completed weeks includes infants born between 36-0 and 36-6 inclusive); b Denominators based on the number of ongoing pregnancies.


The gestational age-specific rates of SGA for ongoing pregnancies were calculated for each completed week of gestation as:

\[
\text{Rate of SGA} = \frac{\text{Number of SGA/Number of infants delivered after induction}}{1000}
\]

The gestational age-specific rates of SGA, serious neonatal morbidity, and neonatal mortality. SGA was defined as less than the 3rd percentile and as less than the 10th percentile of growth. Serious neonatal morbidity was defined as a composite outcome, which included any of the following: seizures, severe respiratory morbidity, sepsis, intracranial hemorrhage, necrotizing enterocolitis, or 5-minute Apgar score ≤3. The components of the neonatal composite were chosen because each of the events was very strongly associated with death and serious disability in long-term follow-up studies. Cesarean delivery after induction of labor was examined as a secondary outcome.

The gestational age-specific rates of stillbirth for ongoing pregnancies of entire cohort of women with gestational hypertension were calculated for each completed week of gestation between 36 and 41 weeks as:

\[
\text{Rate of stillbirth} = \frac{\text{Number of stillbirths/Number of ongoing pregnancies}}{1000}
\]

The gestational week-specific rates of maternal and neonatal morbidity and mortality for live births after induction of labor were calculated for each completed week of gestation between 36 and 42 weeks, which was defined as:

\[
\text{Rate of maternal morbidity/mortality} = \frac{\text{Number of mothers (or infants) with serious morbidity and mortality delivered after induction}}{\text{Number of infants delivered after induction}} \times 1000
\]

Pointwise 95% CI were calculated around each of these gestational age-specific rates. Statistical analyses were performed using FREQ, GLM, and LOGISTIC procedures in SAS 9.2 (SAS Institute Inc, Cary, NC).

Results
The electronic database included 228,668 deliveries. After exclusions for comorbidities and multiple gestations, there were a total of 3588 gravidas ≥36 weeks with gestational hypertension that met inclusion criteria. Table 1 describes the maternal characteristics of this cohort. Women with gestational hypertension...
had a mean admitting BP of 140.3 ± 13.4 mm Hg systolic/86.1 ± 11.7 mm Hg diastolic, and mean arterial BP 104.2 mm Hg ± 11.1.

The numbers of ongoing pregnancies and stillbirth rates for the overall gestational hypertension cohort are provided in Table 2. For those women undergoing induction of labor, the live births, cases of maternal and neonatal morbidity and mortality, along with rates, and 95% CIs for maternal and neonatal morbidity and mortality are also noted in Table 2. There were no maternal deaths in our study cohort. There were only 3 stillbirths in our study cohort, 2 occurring at 37-weeks’ and 1 at 38-weeks’ gestation. After induction, the rate of maternal morbidity reached a nadir of 89.9 per 1000 live births (95% CI, 68.1–111.8) at 38-38 6/7 weeks’ gestation, although the rate of neonatal morbidity and mortality fell to 10.5 per 1000 live births (95% CI, 2.8–18.2) at 39-39 6/7 weeks.

The rates of SGA after induction of labor are displayed in Table 3. The rate of SGA ≤10th percentile decreased sharply between 36- and 37-weeks’ gestation, from 115.6 (95% CI, 73.8–157.3) to 53.0 (95% CI, 31.9–74.1). The rate of SGA ≤3rd percentile reached a nadir of 11.9 between 39- and 39-6/7 weeks’ gestation (95% CI, 3.7–20.2) and then sharply rose to a rate of 25.5 between 40- and 40-6/7 weeks’ gestation (95% CI, 2.8–111.8). Table 4 demonstrates the cesarean delivery rate per 1000 inductions. What is notable is that the rate sharply increases from 286.5 (95% CI, 239.6–335.5) to 407.4 (95% CI, 276.4–538.5) between 40- and 41-weeks’ gestation. The majority of indications for the cesarean deliveries at 41-weeks’ gestation were cephalopelvic disproportion and fetal distress.

**COMMENT**

The goal of our investigation was to quantify and contrast the risks associated with ongoing pregnancy vs induction of labor to determine the optimal timing of delivery in women with gestational hypertension. Analysis of data from this multicenter electronic database demonstrated that induction of labor at 38 weeks was associated with a greatly re-

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**TABLE 4**

<table>
<thead>
<tr>
<th>Cesarean deliveries per 1000 inductions</th>
<th>Gestational age, wks²</th>
<th>Variable</th>
<th>Cesarean sections, n</th>
<th>Cesarean section rate [95% CI]</th>
<th>Cesarean indication, n (%)</th>
<th>Cephalopelvic disproportion</th>
<th>Fetal distress</th>
<th>Elective</th>
<th>Hypertensive disease</th>
<th>Other²</th>
<th>Note</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>36</td>
<td>37</td>
<td>38</td>
<td>39</td>
<td>40</td>
<td>41</td>
<td>≥42</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Live births</td>
<td>226</td>
<td>435</td>
<td>656</td>
<td>670</td>
<td>356</td>
<td>54</td>
<td>4</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cesarean sections, n</td>
<td>56</td>
<td>95</td>
<td>131</td>
<td>160</td>
<td>102</td>
<td>22</td>
<td>2</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cesarean section rate [95% CI]</td>
<td>247.8[191.5–304.1]</td>
<td>218.4[179.6–257.2]</td>
<td>194.7[169.1–220.3]</td>
<td>238.8[206.5–271.1]</td>
<td>286.5[239.6–333.5]</td>
<td>407.4[276.4–538.5]</td>
<td>500[10.0–990.0]</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cesarean indication, n (%)</td>
<td>33 (58.9)</td>
<td>48 (60.5)</td>
<td>33 (63.4)</td>
<td>48 (63.4)</td>
<td>33 (63.4)</td>
<td>33 (63.4)</td>
<td>33 (63.4)</td>
<td></td>
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<td></td>
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</tr>
<tr>
<td>Cephalopelvic disproportion</td>
<td>33 (58.9)</td>
<td>48 (60.5)</td>
<td>33 (63.4)</td>
<td>48 (63.4)</td>
<td>33 (63.4)</td>
<td>33 (63.4)</td>
<td>33 (63.4)</td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Fetal distress</td>
<td>21 (32.1)</td>
<td>15 (22.6)</td>
<td>22 (18.1)</td>
<td>22 (18.1)</td>
<td>22 (18.1)</td>
<td>22 (18.1)</td>
<td>22 (18.1)</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Elective</td>
<td>13 (21.4)</td>
<td>6 (6.3)</td>
<td>6 (6.3)</td>
<td>6 (6.3)</td>
<td>6 (6.3)</td>
<td>6 (6.3)</td>
<td>6 (6.3)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypertensive disease</td>
<td>13 (21.2)</td>
<td>15 (9.4)</td>
<td>15 (9.4)</td>
<td>15 (9.4)</td>
<td>15 (9.4)</td>
<td>15 (9.4)</td>
<td>15 (9.4)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other²</td>
<td>5 (8.9)</td>
<td>7 (7.4)</td>
<td>6 (4.6)</td>
<td>6 (4.6)</td>
<td>6 (4.6)</td>
<td>6 (4.6)</td>
<td>6 (4.6)</td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Note</td>
<td>12 (21.5)</td>
<td>13 (13.7)</td>
<td>13 (13.7)</td>
<td>13 (13.7)</td>
<td>13 (13.7)</td>
<td>13 (13.7)</td>
<td>13 (13.7)</td>
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</tr>
</tbody>
</table>

CI, confidence interval; GA, gestational age. *Cervical ripening before induction of labor is used for singleton gestations. **Cesarean vs vaginal delivery is defined as any cesarean section that was performed during or after the index pregnancy. It includes both those performed during the index pregnancy and those performed after the index pregnancy. Note that multiple codes could be used for a given patient.
duced risk of serious maternal morbidity, and delaying induction of labor until 39 weeks resulted in the lowest risk for SGA <3rd and 10th percentile along with the lowest composite neonatal morbidity and mortality. Induction of labor at 39-weeks’ gestation may be a reasonable option in a woman whose blood pressure is well-controlled with reassuring antenatal testing and an appropriate for gestational age fetus.

To our knowledge this is the first investigation to exclusively study a large cohort of women with gestational hypertension to assess the optimal timing of delivery by quantifying the risks of both adverse maternal and fetal outcomes associated with ongoing pregnancy and with induction of labor. We were concerned with the rising rates of induction of labor at 37 weeks for mild hypertensive disease and questioned whether this was justified. We hypothesized that maternal and neonatal risks would decrease at each advancing gestational week at or near term, but would increase postterm. However, contrary to what we had anticipated, the rate of maternal morbidity reached a nadir between 38- and 38-6/7 weeks’ gestation, and the rates of SGA <3rd and 10th percentiles were lowest at 39-39 6/7 weeks. The composite rate of neonatal morbidity and mortality did decrease as expected, and had a nadir between 39- and 39-6/7 weeks’ gestation.

We also performed the analysis with multiples included in the cohort (65 pairs of twins and 1 set of triplets) and found the same results in regard to when the nadir of maternal and neonatal morbidity occurred. Of note, however, there were 8 more stillbirths in our cohort when multiples were included, with 2-3 stillbirths occurring per week between 36- and 40-weeks’ gestation. Although the numbers are few and further investigation is required, this finding supports that women with gestational hypertension and multiple gestation may benefit from delivery sooner than those with singletons to prevent stillbirth.

Our findings differ from those of the HYPITAT trial, which randomized women with either gestational hypertension or mild preeclampsia presenting between 36- and 41-6/7 weeks’ gestation to either expectant management or induction of labor.4 Adverse maternal outcomes were reduced significantly in women randomized to induction at or beyond 37-0/7; however, we noted that 38-38 6/7 weeks was the optimal time for induction from the maternal perspective. However, Koopmans et al.11 did not separate those gravidas with gestational hypertension, as we did, from those with mild preeclampsia, making it unclear whether morbidities were similar and recommendations should be the same for both diseases.

This is a retrospective analysis of more than 3000 singleton deliveries of women with gestational hypertension from a multicenter database that was drawn from centers across the country, allowing us to assess less frequent outcomes on a week-by-week basis such as maternal abruption, ICU admission rates, postpartum hypertension, seizures, and mortality. We excluded women with comorbidities (eg, diabetes mellitus, renal, or cardiac complications) in an attempt to produce a homogeneous group of women with uncomplicated gestational hypertension. Moreover, on admission no patient in our gestational hypertension cohort had a BP that exceeded 160/110 mm Hg, supporting a milder disease process. Another strength of this study is that the electronic data were verified and correlated highly with chart review, as demonstrated by Zhang et al.10 However, our work is also subject to the pitfalls of a retrospective analysis, such as selection bias. In the current investigation, diagnoses were assigned at admission to the hospital for delivery, and data were not collected on the progression of disease, except for the development of postpartum worsening of hypertension; previously we documented that there were no seizures in any woman with gestational hypertension in this database.12 Thus, we were unable to assess those women with gestational hypertension who may have progressed to preeclampsia. Another potential weakness, common to electronic databases, is incomplete data entry at each site, which may result in type II errors.

In conclusion, induction of labor between 38 to 39 weeks in women with gestational hypertension results in the lowest maternal and neonatal morbidity and mortality. Our findings provide insight regarding the timing of delivery in women with gestational hypertension, and may also provide future direction for a randomized controlled trial in women with gestational hypertension to provide confirmatory evidence.

REFERENCES
12. Cruz MO, Gao W, Hibbard JU. Obstetrical and perinatal outcomes among women with gestational hypertension, mild preeclampsia,


