Original Research

Timing of Delivery in Women With Chronic Hypertension

Maya Ram, MD, Howard Berger, MD, Michael Geary, MD, Sarah D. McDonald, MD, Beth Murray-Davis, PhD, Catherine Riddell, BASc, Haroon Hasan, MPH, Jon Barrett, MD, and Nir Melamed, MD, for the Diabetes, Obesity and Hypertension in Pregnancy Research Network (DOH-NET) and the Southern Ontario Obstetrical Network (SOON) Investigators

OBJECTIVE: To assess whether routine induction of labor at 38 or 39 weeks in women with chronic hypertension is associated with the risk of superimposed preeclampsia or cesarean delivery.

METHODS: We conducted a retrospective population-based study of women with chronic hypertension who had a singleton hospital birth at 38 0/7 weeks of gestation of gestation in Ontario, Canada, between 2012 and 2016. Women who underwent induction of labor at 38 0/7 to 38 6/7 weeks of gestation for chronic hypertension (n=281) were compared with those who were managed expectantly during that week and remained undelivered at 39 0/7 weeks of gestation (n=1,606). Separately, women who underwent induction of labor at 39 0/7 to 39 6/7 weeks of gestation for chronic hypertension (n=259) were compared with women who remained undelivered at 40 0/7 weeks of gestation (n=801).

RESULTS: Of 534,529 women gave birth during the study period, 6,054 (1.1%) had chronic hypertension and 2,420 met the inclusion criteria. Women managed expectantly at 38 or 39 weeks of gestation were at risk of new-onset superimposed preeclampsia (19.2% [308/1,606] and 19.0% [152/801], respectively) and eclampsia (0.6% [10/1,606] and 0.7% [6/801], respectively), and more than half underwent induction of labor later in gestation (56.8% and 57.8%, respectively). The risk of cesarean delivery in the induction groups was lower (38 weeks of gestation) or similar (39 weeks of gestation) to that observed in women managed expectantly at the corresponding weeks (38 weeks of gestation: 17.1% vs 24.0%, adjusted relative risk 0.74 [95% CI 0.57–0.95]; 39 weeks of gestation: 20.1% vs 26.0%, adjusted relative risk 0.90 [95% CI 0.69–1.17]).

CONCLUSION: Our findings suggest that in women with isolated chronic hypertension, induction of labor at 38 or 39 weeks of gestation may prevent severe hypertensive complications without increasing the risk of cesarean delivery.

(Obstet Gynecol 2018;132:669–77)

DOI: 10.1097/AOG.0000000000002800

Chronic hypertension complicates between 1% and 5% of pregnancies,[1,2] and this proportion is expected to rise given the increasing prevalence of obesity

From the Division of Maternal-Fetal Medicine, Department of Obstetrics and Gynecology, Sunnybrook Health Sciences Centre, University of Toronto, Ontario, Canada; the Department of Obstetrics and Gynecology, Lis Hospital for Women, Tel Aviv Sourasky Medical Center, Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel; the Division of Maternal-Fetal Medicine, Department of Obstetrics and Gynecology, St. Michael's Hospital, University of Toronto, Toronto, the Division of Maternal-Fetal Medicine, Departments of Obstetrics and Gynecology, Radiology, and Health Research Methods, Evidence & Impact, McMaster University, Hamilton,and the Better Outcomes Registry & Network (BORN) Ontario, Children's Hospital of Eastern Ontario (CHEO), Ottawa, Ontario, Canada.

Funded by Canadian Institute of Health Research (CIHR) (Grant #146442; Non-communicable Diseases in Obstetrics: Improving Quality of Care and Maternal-infant Outcomes Through an Obstetrical Research Network). Dr. Sarah D. McDonald is supported by a Tier II Canada Research Chair. Dr Beth Murray-Davis is supported by a Hamilton Health Sciences Early Career Award.

Presented as a poster at the annual meeting of the Society for Maternal-Fetal Medicine, January 29–February 3, 2018, Dallas, Texas.

None of the funding agencies had any role in the idea, design, analyses, interpretation of data, writing of the manuscript, or decision to submit the manuscript.

The authors thank Karizma Mawjee for her dedicated contribution as a research coordinator for this project.

Each author has indicated that he or she has met the journal's requirements for authorship.

Received April 13, 2018. Received in revised form May 31, 2018. Accepted June 15, 2018.

Corresponding author: Maya Ram, MD, Division of Maternal-Fetal Medicine, Department of Obstetrics and Gynecology, Sunnybrook Health Sciences Center, 2075 Bayview Avenue, Toronto, Ontario M4N 3M, Canada; email: maya3000@gmail.com.

Financial Disclosure

The authors did not report any potential conflicts of interest.

ISSN: 0029-7844/18

and the increase in maternal age.[3–5] Women with chronic hypertension are at increased risk of adverse pregnancy outcomes including superimposed preeclampsia, fetal growth restriction, placental abruption, and preterm birth, which result in increased maternal and perinatal morbidity and mortality.[2,5–11]

One of the major controversies regarding the management of pregnancies complicated by chronic hypertension relates to the optimal timing of delivery. A policy of a routine induction of labor before 40 weeks of gestation has the potential to decrease the risk of superimposed preeclampsia, placental abruption, and stillbirth. The main concern with such a policy has traditionally been an increased risk of cesarean delivery secondary to failed induction of labor. However, data from low-risk pregnancies[12–14] suggest that such a policy may not increase and may even decrease the risk of cesarean delivery.[15] Another potential concern is that planned early delivery might increase the risk of perinatal morbidity when performed before 39 weeks of gestation.[16–18] Finally, a policy of routine induction of labor has implications with respect to costs and resource use.

Unfortunately, data regarding the benefits and risks of routine induction of labor in women with chronic hypertension are scarce.[19–21] Furthermore, interpretation of available studies is limited by the lack of an adequate control group[19,20,22]; lack of adjustment for potential confounding variables such as maternal body mass index (BMI, calculated as weight (kg)/[height (m)]^2) or parity[20,22]; the inclusion of women with comorbidities or women who underwent induction of labor before 37 weeks of gestation and were thus likely to have been induced for reasons other than chronic hypertension[19,20]; and by small sample size.[21] As a result, the optimal timing of delivery in women with chronic hypertension is currently unclear.

Therefore, our aim was to test the hypothesis that routine induction of labor at 38 or 39 weeks of gestation in women with chronic hypertension may decrease the risk of superimposed preeclampsia and the associated maternal and perinatal complications without increasing the rate of cesarean delivery.

MATERIALS AND METHODS

This was a retrospective population-based study of all women with chronic hypertension who had a singleton hospital birth at 38 0/7 weeks of gestation or greater in Ontario, Canada, between April 2012 and March 2016. Data were obtained from the Better Outcomes Registry & Network (BORN) Ontario (https://www.bornontario.ca/en/about-born/). Better Outcomes Registry & Network Ontario is a province-wide registry of all births in Ontario, Canada. Whenever a woman is admitted to hospital to give birth, data are collected by health care providers and hospital staff from charts, clinical forms and patient interview, and then entered into the Better Outcomes Registry & Network Information System (either directly or by electronic upload from a hospital's electronic medical record system). The Better Outcomes Registry & Network Information System contains maternal demographics, health behaviors, and reproductive history as well as clinical information related to pregnancy, labor, birth, and fetal and neonatal outcomes. An ongoing program of data verifications, quality checks, and formal training sessions for individuals collecting and entering data assures a high level of data quality is maintained. The current study was approved by the Sunnybrook Health Sciences Center Research Ethics Board before the start of the study.

The Better Outcomes Registry & Network Information System was supplemented with a linked copy of the Discharge Abstract Database, which contains a set of validated diagnostic codes from the International Statistical Classification of Diseases and Related Health Problems, 10th Revision, Canadian Version and intervention codes from the Canadian Classifications of Health Interventions for all in-hospital deliveries. The Discharge Abstract Database data were available for most of the study period (fiscal years 2012–2013 to 2014–2015, but not for 2015–2016). This was done for two main reasons: 1) to ensure the highest probability of identifying maternal diagnoses (pre-existing hypertension and diabetes) and 2) because the Better Outcomes Registry & Network Information System currently captures neonatal outcomes occurring in the neonatal intensive care units (NICUs) from all level II special care nursery units (42 units) but only three of the eight level III units. Thus, neonatal data are missing for 5 of 50 NICUs. The linkage with the Discharge Abstract Database therefore was used to compensate for this limitation.

To create a cohort of "low-risk" women with chronic hypertension, women with any of the following conditions were excluded from the study: gestational age at birth greater than 42 0/7 weeks; women who were not candidates for vaginal birth (eg, nonvertex presentation, placenta previa) or had a previous cesarean delivery; women who had stillbirth during the antepartum period; women with chronic medical or pregnancy-related conditions that could potentially influence the decision to induce labor before 40 weeks of gestation including pregestational or gestational diabetes, chronic renal disease, cardiac disease,

pulmonary disease, autoimmune conditions, or hematologic diseases; and major fetal congenital anomalies (Fig. 1).

The choice of the control groups was made to simulate the decision faced by physicians with regard to timing of delivery in real life situations, that is, induction of labor compared with expectant management, with the latter option carrying a risk of new onset of pregnancy complications as well as the potential for labor induction at a later stage of

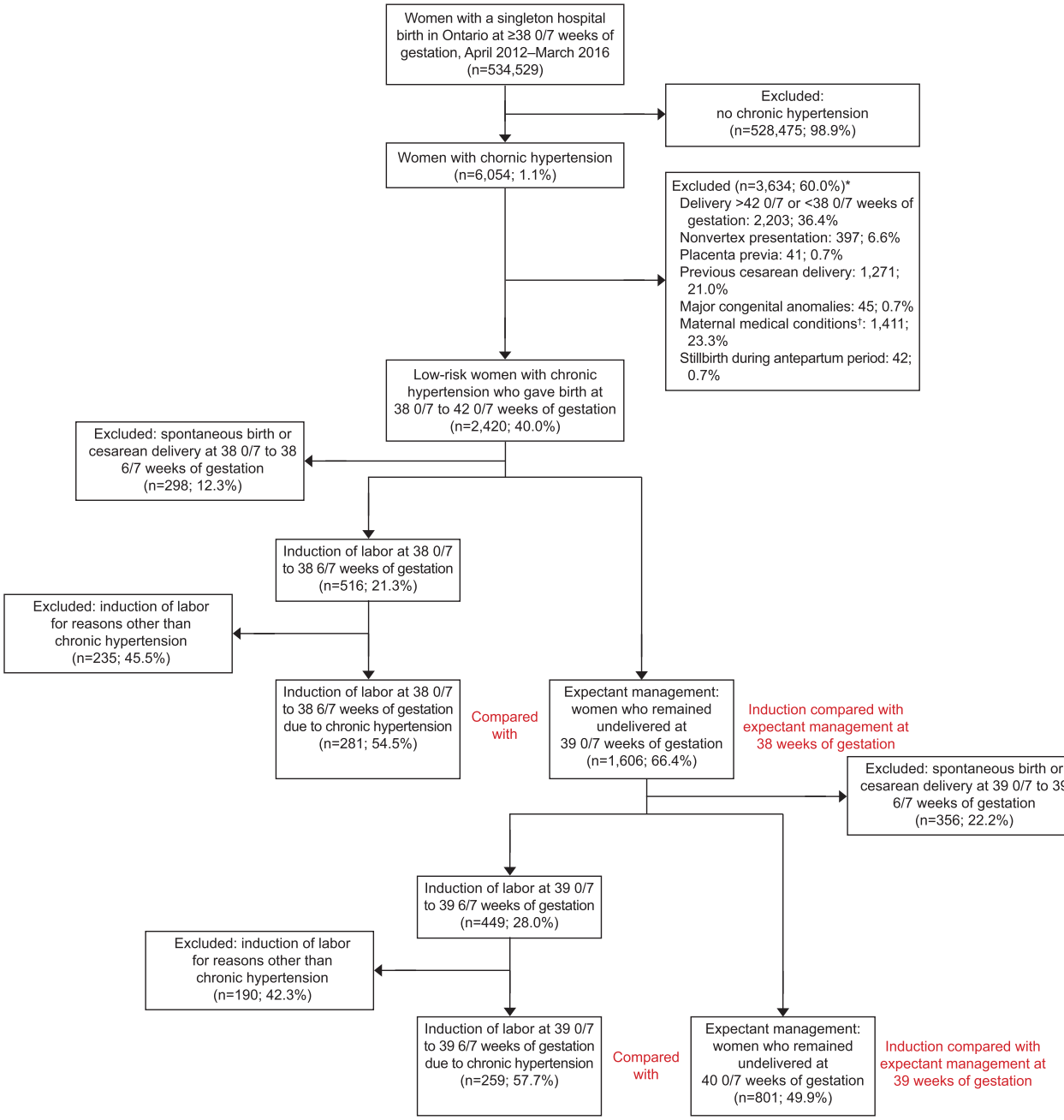

Fig. 1. Description of the study and control groups. *Not mutually exclusive. †Pregestational or gestational diabetes, chronic renal disease, cardiac disease (congenital or acquired), pulmonary disease (pulmonary hypertension, cystic fibrosis, pulmonary embolism), autoimmune conditions (systemic lupus erythematosus), and hematologic diseases (hemophilia, sickle cell disease).

Ram. Induction of Labor in Chronic Hypertension. Obstet Gynecol 2018.

gestation. Thus, we compared women who underwent induction of labor at 38 0/7 to 38 6/7 weeks of gestation ("38-IOL group") with those managed expectantly during the corresponding week and remained undelivered until 39 0/7 weeks of gestation (ie, gave birth between 39 0/7 and 42 0/7 weeks of gestation) ("38-Expectant group"). We performed a separate comparison between women who underwent induction of labor at 39 0/7 to 39 6/7 weeks of gestation ("39-IOL group") and those managed expectantly during the corresponding week and remained undelivered until 40 0/7 weeks of gestation (ie, gave birth between 40 0/7 and 42 0/7 weeks of gestation) ("39-Expectant group") (Fig. 1). Only women whose sole documented reason for induction of labor was chronic hypertension were included in the 38-IOL and 39-IOL groups (Fig. 1). Women who underwent induction of labor for reasons other than chronic hypertension and women who experienced spontaneous delivery or primary cesarean delivery were excluded from the analysis (Fig. 1).

The Society of Obstetricians and Gynecologists of Canada,[23] similar to the American College of Obstetricians and Gynecologists,[24] defines chronic hypertension as hypertension (blood pressure 140/90 mm Hg or greater) that developed either before pregnancy or that was diagnosed before 20 weeks of gestation. Superimposed preeclampsia is defined by the Society as the development of one or more of the following complications at 20 weeks of gestation or greater in women with chronic hypertension: resistant hypertension, new or worsening proteinuria, or severe complications related to preeclampsia including central nervous system, cardiorespiratory, hematologic, renal, hepatic, or placental complications.[23] Small for gestational age was defined as birth weight less than the 10th percentile for gestational age based on sex-specific national references.[25]

The primary outcome was the rate of superimposed preeclampsia in the expectant management groups. As per study design, the rate of superimposed preeclampsia in the induction of labor groups was zero; the study question was focused on women undergoing induction of labor for isolated chronic hypertension. Secondary maternal outcomes were cesarean and instrumental delivery and labor induction in the expectant management groups. Secondary perinatal outcomes were stillbirth and neonatal mortality and morbidity. Neonatal respiratory morbidity was defined as any of the following: need for respiratory support in the form of continuous positive airway pressure or mechanical ventilation, a diagnosis of transient tachypnea of the newborn, or respiratory distress syndrome. Composite neonatal morbidity was defined as the presence of any of the following: perinatal mortality (stillbirth or neonatal death), 5-minute Apgar score less than 7, admission to a NICU, neonatal respiratory morbidity (as defined previously), hypoglycemia, or jaundice requiring phototherapy.

Detailed information regarding the methods used to determine the estimated gestational age is not available given the population-based design. However, the Society of Obstetricians and Gynaecologists of Canada recommends that all pregnant women should have a first-trimester ultrasonogram and that determination of gestational age should be based on the results of first- or second-trimester ultrasonogram except for pregnancies conceived by assisted reproductive technology.[26]

Characteristics and outcomes were compared between the induction and expectant management groups using the Mann-Whitney *U* test for continuous variables and the χ^2 and Fisher exact test for categorical variables, as appropriate. Multivariable modified Poisson regression analysis with robust error variance was used to calculate the risk ratios for maternal and neonatal complications in women who underwent induction of labor at 38 or 39 weeks of gestation (using women managed expectantly at the corresponding weeks as reference) while adjusting for potential confounding variables including maternal age, parity, and prepregnancy BMI. A subgroup analysis was conducted in nulliparous women because the results of induction of labor and the risk of pregnancy-related hypertensive complications vary between nulliparous and multiparous women.

Data were analyzed using the SAS 9.4. Significance was set at a two-sided *P* value $<.05$.

RESULTS

A total of 534,529 women with singleton pregnancies had a hospital birth in Ontario, Canada, during the study period, of whom 6,054 (1.1%) had chronic hypertension and 2,420 met the study inclusion criteria (Fig. 1). The 281 women who underwent induction of labor at 38 0/7 to 38 6/7 weeks of gestation as a result of chronic hypertension (38-IOL group) were compared with 1,606 women who were managed expectantly during the corresponding week and remained undelivered until at least 39 0/7 weeks of gestation (38-Expectant group). Similarly, 259 women who underwent induction of labor at 39 0/7 to 39 6/7 weeks of gestation as a result of chronic hypertension (39-IOL group) were compared with 801 women who remained undelivered until at least 40 0/7 weeks of gestation (39-Expectant group) (Fig. 1).

Overall, the characteristics of women in the induction and expectant management groups were similar with regard to maternal age, parity, and BMI with the exception of a lower proportion of overweight women (BMI 25.0–29.9) in the 39-Expectant group compared with the 39-IOL group (Table 1).

Women managed expectantly at 38 or 39 weeks of gestation were at risk of new onset of superimposed preeclampsia (19.2% and 19.0%, respectively) and eclampsia (0.6% and 0.7%, respectively) (Table 2). The proportion of women in the 38-Expectant and 39-Expectant groups who underwent subsequent induction of labor was 56.8% and 57.8%, respectively (Table 2). The rate of placental abruption was too low to be analyzed.

Women in the 38-IOL group had a lower rate of cesarean delivery compared with those in the 38-Expectant group (17.1% vs 24%, P=.011); whereas the difference in cesarean delivery rate between women in the 39-IOL and 39-Expectant groups was not statistically significant (20.1% vs 26%, P=.056) (Table 2).

As expected per study design, neonates of mothers in the 38-IOL and 39-IOL groups were born at an earlier gestational age and had a lower median birth weight compared with neonates of mothers managed expectantly at the corresponding weeks (Table 3). However, the proportion of small-for-gestational-age neonates was similar between the induction and expectant management groups (Table 3).

Neonates in the 39-IOL group had a lower rate of respiratory morbidity compared with those in the 39-Expectant group (6.2% vs 11.9%, P=.009). Otherwise, there were no differences between the groups with regard to composite neonatal morbidity, admission to a NICU, jaundice requiring phototherapy, and neonatal hypoglycemia (Table 3).

The findings described persisted after adjustment for maternal age, parity, and maternal prepregnancy BMI (Table 4). Women in the 38-IOL group had a lower risk for cesarean delivery compared with women in the 38-Expectant group (adjusted relative risk 0.74, 95% CI 0.57–0.95); whereas the risk of cesarean delivery for women in the 39-IOL group was not different than that of women in the 39-Expectant group (adjusted relative risk 0.90, 95% CI 0.69–1.17). Neonates in the 39-IOL group had a lower risk of respiratory morbidity compared with neonates in the 39-Expectant group (adjusted relative risk 0.49, 95% CI 0.28–0.85) (Table 4).

Given that the risk of superimposed preeclampsia and the risk of induction failure may be higher in nulliparous women, we repeated the adjusted analysis in the subgroup of nulliparous women. There was no significant difference in the risk of cesarean delivery in women undergoing induction of labor at 38 or 39 weeks of gestation compared with women managed expectantly during the corresponding weeks in the subgroup of nulliparous women (Table 4).

DISCUSSION

The main finding of the current study is that, in women with isolated chronic hypertension, induction of labor at 38 or 39 weeks of gestation may avoid the

Table 1. Characteristics of the Women in the Induction and Expectant Management Groups

	38 Wk of Gestation			39 Wk of Gestation		
Characteristic	Induction (n=281)	Expectant Management (n=1,606)	*P*	Induction (n=259)	Expectant Management (n=801)	*P*
Maternal age (y)	32 (29–35)	32 (29–36)	.425	32 (29.0–36.0)	32.0 (28.0–36.0)	.080
Older than 35	75 (26.7)	462 (28.8)	.476	79 (30.5)	216 (27.0)	.269
Nulliparity	153 (54.4)	884 (55.0)	.853	143 (55.2)	478 (59.7)	.205
BMI (kg/m^2)	30.5 (25.2–35.8)	29.0 (24.4–34.7)	.106	29.0 (25.1–34.5)	29.8 (24.7–35.3)	.567
Less than 18.5	Less than 6*	23 (1.4)	N/A	Less than 6*	13 (1.6)	N/A
18.5–24.9	55 (19.6)	380 (23.7)	.133	53 (20.5)	177 (22.1)	.579
25.0–29.9	54 (19.2)	385 (24.0)	.082	71 (27.4)	171 (21.3)	**.043**
30.0 or greater	131 (46.6)	651 (40.5)	.056	104 (40.2)	348 (43.4)	.352
Female newborn	144 (51.2)	769 (47.9)	.298	135 (52.1)	381 (47.6)	.202

BMI, body mass index; N/A, nonapplicable.
Data are median (interquartile range) or n (%) unless otherwise specified.
Bold indicates significant *P* values.
* As per the policy of the Better Outcomes Registry & Network Ontario Registry, values are not shown when the cell count is lower than 6.

Table 2. Pregnancy Outcomes in the Induction and Expectant Management Groups

Outcome	38 Wk of Gestation			39 Wk of Gestation		
	Induction (n=281)	Expectant Management (n=1,606)	*P*	Induction (n=259)	Expectant Management (n=801)	*P*
Superimposed preeclampsia	0 (0.0)*	308 (19.2)	**<.001**	0 (0.0)*	152 (19.0)	**<.001**
Eclampsia	0 (0.0)*	10 (0.6)	**<.001**	0 (0.0)*	6 (0.7)	**<.001**
Placental abruption	Less than 6†	6 (0.4)	N/A	Less than 6†	Less than 6†	N/A
Labor induction	281 (100)	912 (56.8)	**<.001**	259 (100)	463 (57.8)	**<.001**
Epidural	208 (74.0)	1,177 (73.3)	.800	196 (75.7)	596 (74.4)	.683
Cesarean delivery	48 (17.1)	385 (24.0)	**.011**	52 (20.1)	208 (26.0)	.056
Instrumental delivery	34 (12.1)	205 (12.8)	.757	36 (13.9)	97 (12.1)	.450
Postpartum hemorrhage	Less than 6†	56 (3.5)	N/A	7 (2.7)	29 (3.6)	.478

N/A, nonapplicable.
Data are n (%) unless otherwise specified.
Bold indicates significant *P* values.
* As per study design, the induction groups included women for whom the only indication for induction of labor was chronic hypertension to simulate a policy of routine induction of labor in women with chronic hypertension. Thus, women with superimposed preeclampsia were excluded from the induction groups.
† As per the policy of the Better Outcomes Registry & Network Ontario Registry, values are not shown when the cell count is lower than 6.

Table 3. Neonatal Outcomes in the Induction and Expectant Management Groups

Outcome	38 Wk of Gestation			39 Wk of Gestation		
	Induction (n=281)	Expectant Management (n=1,606)	*P*	Induction (n=259)	Expectant Management (n=801)	*P*
Gestational age at birth (wk)	38.4 (38.1–38.7)	39.9 (39.4–40.4)	**<.001**	39.3 (39.1–39.6)	40.4 (40.1–40.9)	**<.001**
Birth weight (g)	3,161 (2,867–3,506)	3,460 (3,157–3,778)	**<.001**	3,306 (3,078–3,640)	3,580 (3,235–3,855)	**<.001**
Less than the 10th percentile*	33 (11.7)	180 (11.2)	.966	28 (10.8)	90 (11.2)	.922
Composite neonatal outcome†	61 (21.7)	316 (19.7)	.432	46 (17.8)	164 (20.5)	.341
Perinatal mortality	Less than 6§	Less than 6§	N/A	Less than 6§	Less than 6§	N/A
5-min Apgar score less than 7	7 (2.5)	37 (2.3)	.947	Less than 6§	25 (3.1)	N/A
Respiratory morbidity‡	28 (10.0)	152 (9.5)	.792	16 (6.2)	95 (11.9)	**.009**
Respiratory distress syndrome	13 (4.6)	53 (3.3)	.264	Less than 6§	32 (4.0)	N/A
NICU admission	27 (9.6)	180 (11.2)	.429	26 (10.0)	95 (11.9)	.423
Length of stay in NICU (d)	2.9 (1.4–5.6)	2.6 (1.0–4.7)	.279	2.2 (1.4–3.0)	2.4 (1.0–4.4)	.892
Jaundice requiring phototherapy	20 (7.1)	71 (4.4)	.052	16 (6.2)	28 (3.5)	.060
Hypoglycemia	9 (3.2)	38 (2.4)	.406	Less than 6§	19 (2.4)	N/A

N/A, nonapplicable; NICU, neonatal intensive care unit.
Data are median (interquartile range) or n (%) unless otherwise specified.
Bold indicates significant *P* values.
* Based on national sex-specific birth weight reference.[25]
† Composite neonatal outcome is defined as any of the following: perinatal mortality, 5-min Apgar score less than 7, admission to the NICU, neonatal respiratory morbidity, jaundice requiring phototherapy, or hypoglycemia.
‡ Respiratory morbidity is defined as any of the following: respiratory distress syndrome, transient tachypnea of the newborn, or need for respiratory support.
§ As per the policy of the Better Outcomes Registry & Network Ontario Registry, values are not shown when the cell count is lower than 6.

Table 4. Association of Labor Induction (Compared With Expectant Management) With Adverse Maternal and Neonatal Outcomes—Multivariable Analysis

	Likelihood of Outcome in the Induction Group (Using the Expectant Management Group as a Reference)			
	At 38 Wk of Gestation		At 39 Wk of Gestation	
Outcome	Crude RR (95% CI)	Adjusted RR (95% CI)*	Crude RR (95% CI)	Adjusted RR (95% CI)*
Overall group				
Cesarean delivery	**0.71 (0.54–0.93)**	**0.74 (0.57–0.95)**	0.78 (0.60–1.02)	0.90 (0.69–1.17)
Composite neonatal outcome†	1.10 (0.87–1.41)	1.10 (0.85–1.42)	0.87 (0.65–1.17)	0.85 (0.60–1.20)
NICU admission	0.86 (0.58–1.26)	0.83 (0.55–1.26)	0.85 (0.56–1.28)	0.87 (0.57–1.33)
Respiratory morbidity‡	1.05 (0.72–1.54)	1.06 (0.71–1.59)	**0.52 (0.31–0.86)**	**0.49 (0.28–0.85)**
Nulliparous women				
Cesarean delivery	**0.74 (0.56–0.98)**	0.81 (0.62–1.06)	0.79 (0.57–1.03)	0.86 (0.65–1.13)
Composite neonatal outcome†	0.99 (0.72–1.33)	0.96 (0.7–1.33)	1.05 (0.76–1.44)	1.03 (0.73–1.44)
NICU admission	0.74 (0.46–1.20)	0.66 (0.38–1.14)	1.02 (0.66–1.58)	1.04 (0.65–1.64)
Respiratory morbidity‡	0.76 (0.45–1.28)	0.75 (0.42–1.32)	0.68 (0.39–1.17)	0.67 (0.37–1.20)

RR, relative risk; NICU, neonatal intensive care unit.
Bold indicates significant associations.
* Values are presented as RR (95% CI) and reflect the results of multivariable modified Poisson regression analysis adjusting for potential confounders: maternal age, nulliparity (only in the overall group) and prepregnancy body mass index.
† Composite morbidity is defined as any of the following: perinatal mortality, 5-min Apgar score less than 7, admission to the NICU, hypoglycemia, jaundice requiring phototherapy, or neonatal respiratory morbidity.
‡ Respiratory morbidity is defined as any of the following: respiratory distress syndrome, transient tachypnea of the newborn, or need for respiratory support.

approximate 20% risk of superimposed preeclampsia associated with expectant management during the corresponding weeks without associated increases in the risk of cesarean delivery. Approximately 25% of women with chronic hypertension will develop superimposed preeclampsia,[11] often late in pregnancy.[27] In addition, women with chronic hypertension are at increased risk of other complications such as placental abruption[8] and stillbirth.[20] Thus, the rationale for routine induction of labor in women with chronic hypertension is clear, because such a policy would prevent these complications in women destined to develop these complications later in gestation. However, data on the benefits and risks of routine induction of labor in women with chronic hypertension are scarce[19–21] and are limited by small sample size, lack of an adequate control group, and by lack of information on potential confounding variables. The results of our study, in which we tried to overcome these limitations, provide support for the hypothesis that a policy of routine induction of labor at 38 or 39 weeks of gestation in women with chronic hypertension can prevent the complications described.

Our finding that induction is not associated with an increased the risk of cesarean delivery compared with expectant management is consistent with observational studies of low-risk women undergoing elective induction of labor.[12,13,28] This finding may be attributed to an increased risk of urgent cesarean delivery in the expectant management groups as a result of superimposed preeclampsia and to the fact that more than half of the women in the expectant management groups undergo induction of labor at a more advanced gestational age.

The fact that we did not find differences in maternal morbidity and neonatal morbidity (other than respiratory morbidity at 39 weeks of gestation) between the induction of labor and expectant management groups may be the result of the insufficient sample size. However, based on the association of superimposed preeclampsia with maternal and neonatal morbidity,[2,29,30] we believe that the approximate 20% risk of superimposed preeclampsia in the expectant management groups can be used as a surrogate of adverse maternal and neonatal outcome.

We were able to identify only one randomized controlled study[21] and two retrospective studies[19,20] that compared induction of labor with expectant management in women with chronic hypertension. Hamed et al randomized 76 women with mild to moderate chronic hypertension to induction of labor at 37 weeks of gestation compared with expectant

management until 41 week of gestation. In contrast to our findings, they reported that induction of labor at 37 weeks of gestation was associated with an increased risk of cesarean delivery and admission to the NICU, whereas it did not affect the risk of developing superimposed preeclampsia.[21] However, the interpretation of this study is limited by the small sample size (38 women in each arm) and by the relative early gestational age in the induction of labor group (37 weeks). In a retrospective population-based study, Hutcheon et al[20] found that induction of labor at 38 or 39 weeks of gestation in women with chronic hypertension provided the optimal balance between the competing risks of stillbirth and neonatal mortality and morbidity. The main limitation of that study is that the authors were unable to distinguish between women with uncomplicated chronic hypertension and women with chronic hypertension who developed superimposed preeclampsia. As a result, some of the women who underwent induction of labor were induced for superimposed preeclampsia rather than chronic hypertension. Moreover, the design used by the authors does not provide comparison of induction of labor with expectant management but merely provides week-specific estimates of the risk of stillbirth and neonatal mortality and morbidity. In a more recent small single-center retrospective study, Harper et al[19] reported that, in agreement with our findings, expectant management beyond 39 weeks of gestation in women with chronic hypertension was associated with increased risk of severe preeclampsia. Beyond the small number of women in the induction of labor groups (range 20–124), the interpretation of that study is limited by the fact that they included women with comorbidities in whom induction of labor was performed for reasons other than chronic hypertension so that these findings cannot address the role of routine induction of labor in women with isolated chronic hypertension.

The current study has several limitations. As a result of the population-based design, we did not have information on several potential confounding variables such as the severity of chronic hypertension, maternal ethnicity, and differences in the practice of labor induction and patient populations between individual care providers and medical centers; thus, residual confounding cannot be ruled out. To simulate a policy of routine (or preventive) induction of labor in women with isolated chronic hypertension, we excluded women with the diagnosis of superimposed preeclampsia from the induction of labor groups, which means that per definition, the rate of superimposed preeclampsia in the induction of labor group in our study is zero. We recognize that this approach did not allow us identify women who underwent induction of labor as a result of isolated chronic hypertension but developed superimposed preeclampsia during the process of induction, delivery, or in the postpartum period and that this may result in a statistical bias for the comparison of the rate of superimposed preeclampsia between the induction of labor and expectant management groups. Finally, despite its relatively large sample size, our study is insufficiently powered to assess uncommon maternal and perinatal outcomes such as perinatal mortality, low Apgar scores, and neonatal hypoglycemia.

In summary, we have found that in women with isolated chronic hypertension, induction of labor at 38 or 39 weeks of gestation may prevent severe hypertensive complications without associated increases (or with even associated decreases) in the risk of cesarean delivery and that induction of labor at 39 weeks of gestation is associated with a lower risk of neonatal respiratory morbidity compared with expectant management. Although these findings should be interpreted with caution given the limitations described, we believe that for care providers and women with isolated chronic hypertension who are considering induction of labor before 40 weeks of gestation, the current study may provide support for such a practice. The decision regarding the timing of delivery should be further based on additional factors such as patient preference, the severity of hypertension, history of preeclampsia in previous pregnancies, presence of fetal growth restriction, and factors that may affect the risk of cesarean delivery such as parity and Bishop score.

REFERENCES

1. Sibai BM. Chronic hypertension in pregnancy. Obstet Gynecol 2002;100:369–77.
2. Ahmad AS, Samuelsen SO. Hypertensive disorders in pregnancy and fetal death at different gestational lengths: a population study of 2 121 371 pregnancies. BJOG 2012;119:1521–8.
3. Dayan N, Lanes A, Walker MC, Spitzer KA, Laskin CA. Effect of chronic hypertension on assisted pregnancy outcomes: a population-based study in Ontario, Canada. Fertil Steril 2016;105:1003–9.
4. Leon MG, Moussa HN, Longo M, Pedroza C, Haidar ZA, Mendez-Figueroa H, et al. Rate of gestational diabetes mellitus and pregnancy outcomes in patients with chronic hypertension. Am J Perinatol 2016;33:745–50.
5. Bateman BT, Bansil P, Hernandez-Diaz S, Mhyre JM, Callaghan WM, Kuklina EV. Prevalence, trends, and outcomes of chronic hypertension: a nationwide sample of delivery admissions. Am J Obstet Gynecol 2012;206:134.e1–8.
6. Zetterström K, Lindeberg SN, Haglund B, Hanson U. Maternal complications in women with chronic hypertension: a popula-

tion-based cohort study. Acta Obstet Gynecol Scand 2005;84:419–24.

7. Zetterström K, Lindeberg SN, Haglund B, Hanson U. Chronic hypertension as a risk factor for offspring to be born small for gestational age. Acta Obstet Gynecol Scand 2006;85:1046–50.
8. Ananth CV, Peltier MR, Kinzler WL, Smulian JC, Vintzileos AM. Chronic hypertension and risk of placental abruption: is the association modified by ischemic placental disease? Am J Obstet Gynecol 2007;197:273.e1–7.
9. Zetterström K, Lindeberg SN, Haglund B, Hanson U. The association of maternal chronic hypertension with perinatal death in male and female offspring: a record linkage study of 866,188 women. BJOG 2008;115:1436–42.
10. Ankumah NE, Sibai BM. Chronic hypertension in pregnancy: diagnosis, management, and outcomes. Clin Obstet Gynecol 2017;60:206–214.
11. Bramham K, Parnell B, Nelson-Piercy C, Seed PT, Poston L, Chappell LC. Chronic hypertension and pregnancy outcomes: systematic review and meta-analysis. BMJ 2014;348:g2301.
12. Cheng YW, Kaimal AJ, Snowden JM, Nicholson JM, Caughey AB. Induction of labor compared to expectant management in low-risk women and associated perinatal outcomes. Am J Obstet Gynecol 2012;207:502.e1–8.
13. Darney BG, Snowden JM, Cheng YW, Jacob L, Nicholson JM, Kaimal A, et al. Elective induction of labor at term compared with expectant management: maternal and neonatal outcomes. Obstet Gynecol 2013;122:761–9.
14. Mishanina E, Rogozinska E, Thatthi T, Uddin-Khan R, Khan KS, Meads C. Use of labour induction and risk of cesarean delivery: a systematic review and meta-analysis. CMAJ 2014;186:665–73.
15. Koopmans CM, Bijlenga D, Groen H, Vijgen SM, Aarnoudse JG, Bekedam DJ, et al. Induction of labour versus expectant monitoring for gestational hypertension or mild pre-eclampsia after 36 weeks' gestation (HYPITAT): a multicentre, open-label randomised controlled trial. Lancet 2009;374:979–88.
16. Hansen AK, Wisborg K, Uldbjerg N, Henriksen TB. Risk of respiratory morbidity in term infants delivered by elective caesarean section: cohort study. BMJ 2008;336:85–7.
17. De Luca R, Boulvain M, Irion O, Berner M, Pfister RE. Incidence of early neonatal mortality and morbidity after late-preterm and term cesarean delivery. Pediatrics 2009;123:e1064–71.
18. Tita AT, Landon MB, Spong CY, Lai Y, Leveno KJ, Varner MW, et al. Timing of elective repeat cesarean delivery at term and neonatal outcomes. N Engl J Med 2009;360:111–20.
19. Harper LM, Biggio JR, Anderson S, Tita AT. Gestational age of delivery in pregnancies complicated by chronic hypertension. Obstet Gynecol 2016;127:1101–9.
20. Hutcheon JA, Lisonkova S, Magee LA, Von Dadelszen P, Woo HL, Liu S, et al. Optimal timing of delivery in pregnancies with pre-existing hypertension. BJOG 2011;118:49–54.
21. Hamed HO, Alsheeha MA, Abu-Elhasan AM, Abd Elmoniem AE, Kamal MM. Pregnancy outcomes of expectant management of stable mild to moderate chronic hypertension as compared with planned delivery. Int J Gynaecol Obstet 2014;127:15–20.
22. Broekhuijsen K, Ravelli AC, Langenveld J, van Pampus MG, van den Berg PP, Mol BW, et al. Maternal and neonatal outcomes of pregnancy in women with chronic hypertension: a retrospective analysis of a national register. Acta Obstet Gynecol Scand 2015;94:1337–45.
23. Magee LA, Pels A, Helewa M, Rey E, von Dadelszen P; SOGC Hypertension Guideline Committee. Diagnosis, evaluation, and management of the hypertensive disorders of pregnancy: executive summary. J Obstet Gynaecol Can 2014;36:575–6.
24. American College of Obstetricians and Gynecologists; Task Force on Hypertension in Pregnancy. Hypertension in pregnancy. Report of the American College of Obstetricians and Gynecologists' Task Force on hypertension in pregnancy. Obstet Gynecol 2013;122:1122–31.
25. Kramer MS, Platt RW, Wen SW, Joseph KS, Allen A, Abrahamowicz M, et al. A new and improved population-based Canadian reference for birth weight for gestational age. Pediatrics 2001;108:E35.
26. Butt K, Lim K; Diagnostic Imaging Committee. Determination of gestational age by ultrasound. J Obstet Gynaecol Can 2014;36:171–81.
27. Chappell LC, Enye S, Seed P, Briley AL, Poston L, Shennan AH. Adverse perinatal outcomes and risk factors for preeclampsia in women with chronic hypertension: a prospective study. Hypertension 2008;51:1002–9.
28. Stock SJ, Ferguson E, Duffy A, Ford I, Chalmers J, Norman JE. Outcomes of elective induction of labour compared with expectant management: population based study. BMJ 2012;344:e2838.
29. Tuuli MG, Rampersad R, Stamilio D, Macones G, Odibo AO. Perinatal outcomes in women with preeclampsia and superimposed preeclampsia: do they differ? Am J Obstet Gynecol 2011;204:508.e1–7.
30. Hu WS, Feng Y, Dong MY, He J. Comparing maternal and perinatal outcomes in pregnancies complicated by preeclampsia superimposed chronic hypertension and preeclampsia alone. Clin Exp Obstet Gynecol 2016;43:212–5.