Canadian Stroke Best Practices

CANADIAN STROKE BEST PRACTICE RECOMMENDATIONS

Acute Stroke Management during Pregnancy Consensus Statement

Initial Management

Ladhani NNN, Swartz R H, (Writing Group Chairs), Lindsay MP (Senior Editor)
on Behalf of the Canadian Stroke Best Practice Recommendations
STROKE IN PREGNANCY Writing Group and the
Canadian Stroke Best Practices and Quality Advisory Committees,
in collaboration with the Canadian Stroke Consortium

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Hypertension	
Bushnell C, McCullough LD, Awad IA, Chireau MV, Fedder WN, Furie KL, Howard VJ, Lichtman JH, Lisabeth LD, Piña IL, Reeves MJ, Rexrode KM, Saposnik G, Singh V, Towfighi A, Vaccarino V, Walters MR; on behalf of the American Heart Association Stroke Council, Council on Cardiovascular and Stroke Nursing, Council on Clinical Cardiology, Council on Epidemiology and Prevention, and Council for High Blood Pressure Research. **Guidelines for the prevention of stroke in women: a statement for healthcare professionals from the American Heart Association/American Stroke Association. *Stroke* 2014;45(5):1545-88.**	Treatment of Hypertension in Pregnancy and Postpartum 1. Severe hypertension in pregnancy should be treated with safe and effective antihypertensive medications, such as , with consideration of maternal and fetal side effects (Class I; Level of Evidence A). 2. Consideration may be given to treatment of moderate hypertension in pregnancy with safe and effective antihypertensive medications, given the evidence for possibly increased stroke risk at currently defined systolic and diastolic BP cutoffs, as well as evidence for decreased risk for the development of severe hypertension with treatment (although maternal-fetal risk-benefit ratios have not been established) (Class IIa; Level of Evidence B). 3. Atenolol, angiotensin receptor blockers, and direct renin inhibitors are contraindicated in pregnancy and should not be used (Class III; Level of Evidence C). 4. After giving birth, women with chronic hypertension should be continued on their antihypertensive regimen, with dosage adjustments to reflect the decrease in volume of distribution and glomerular filtration rate that occurs after delivery. They should also be monitored carefully for the development of postpartum preeclampsia (Class IIa; Level of Evidence C).
Magee LA, Pels A, Helewa M, Rey E, von DP. Et al. **Diagnosis, evaluation, and management of the hypertensive disorders of pregnancy: executive summary.** ***J Obstet Gynaecol Can* 2014;36(5):416-441.** **(selected)**	Antihypertensive Therapy for Severe Hypertension Recommendations • Blood pressure should be lowered to < 160 mmHg systolic and < 110 mmHg diastolic. (I-A). • Initial antihypertensive therapy in the hospital setting should be with nifedipine short-acting capsules, parenteral hydralazine, or parenteral labetalol. (I-A) (Table 7). • Alternative antihypertensive medications include a nitroglycerin infusion (I-B), oral methyldopa (I-B), oral labetalol (I-B), oral clonidine (III-B), or postpartum, oral captopril. (III-B). • Refractory hypertension may be treated with sodium nitroprusside. (III-B). • Nifedipine and magnesium sulphate can be used contemporaneously. (II-2B). Magnesium sulphate is not recommended solely as an antihypertensive agent. (I-E) 68. Continuous fetal heart rate monitoring is advised until blood pressure is stable. (III-L)
Hypertension in Pregnancy. Report of the American College of Obstetricians & Gynecologists Task Force on Hypertension in Pregnancy ***Obstetrics & Gynecology* 2013:122:1122-31**	• Close monitoring of women with gestational hypertension or preeclampsia without severe features, with serial assessment of maternal symptoms and fetal movement (daily by the woman), serial measurements of BP (twice weekly), and assessment of platelet counts and liver enzymes (weekly) is suggested. • For women with mild gestational hypertension or preeclampsia with a persistent BP of less than 160 systolic or 110 diastolic, it is suggested that antihypertensive medications not be administered. For women with gestational hypertension or preeclampsia without severe features, it is suggested that strict bed rest not be

Guideline	Recommendations
(selected)	prescribed. • For women with preeclampsia with systolic BP of less than 160 and a diastolic BP less than 110 and no maternal symptoms, it is suggested that magnesium sulfate not be administered universally for the prevention of eclampsia. For women with preeclampsia with severe hypertension during pregnancy (sustained systolic BP of at least 160 or diastolic of at least 110), the use of antihypertensive therapy is recommended.

Evidence Tables

Pre-Eclampsia-Eclampsia

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
Increased Risk of Stroke Associated with Pre-eclampsia/Eclampsia					
Miller et al. 2017 **USA** **Case-control study**	N/A	3,373,144 women, aged 12 to 55 years who were admitted to New York State hospital for any reason from 2003 to 2012 were eligible from the study. Women without preeclampsia were not included in the study, regardless of whether they had a stroke during or after pregnancy. The 197 stroke cases were matched with 591 non-stroke controls. Cases: Women with preeclampsia and pregnancy-related stroke.	Billing data from the New York State Department Health inpatient database was used to identify cases and controls. Women with preeclampsia and pregnancy-related stroke were matched 1 to 3 to preeclamptic controls based on age and race/ethnicity, and insurance status; and were selected randomly from a pool of women with preeclampsia without pregnancy-related stroke.	Stroke	**Events** 88,857 women had preeclampsia, of whom, 197 (0.2%) had a pregnancy-related stroke **Incidence:** Cumulative incidence of pregnancy-related stroke in women with preeclampsia was 222 per 100,000 women during the study period. **Timing** 66.5% occurred post-partum 27.9% stroke antepartum 4.1% strokes occurred during the delivery hospitalization 1.5% occurred during an admission without delivery **In-hospital mortality** 13.2% among cases 0.2% among controls **Factors associated with stroke in women with preeclampsia:** Compared to controls, women with preeclampsia and stroke were more likely to have: Severe preeclampsia or eclampsia: OR: 7.2; 95% CI: 4.6 to 11.3 Infection present on admission: OR: 3.0; 95% CI: 1.6 to 5.8 Prothrombotic states: OR: 3.5; 95% CI: 1.3 to 9.2 Coagulopathies: OR: 3.1; 95% CI: 1.3 to 7.1 Chronic hypertension: OR: 3.2; 95% CI: 1.8 to 5.5 **Factors associated with stroke – Severity-stratified subgroup analysis** ***Mild subgroup:***

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					Chronic hypertension: OR: 3.0; 95% CI: 1.4 to 6.3 Infection present on admission: OR: 4.5; 95% CI: 1.6 to 12.6 ***Severe subgroup:*** Chronic hypertension: OR: 8.4; 95% CI: 3.1 to 22.5 Prothrombotic states: OR: 6.6; 95% CI: 2.5 t 17.5
Ohno et al. 2013 **Japan** **Cross-sectional study**	NA	322,599 deliveries that occurred between 2005 and 2009 in 166 institutions in the Aichi region. This region represents approximately 7% of the Japanese population and 7% of the annual births in Japan.	A questionnaire was sent to all institutions aimed at obtaining information regarding the incidence, management and outcomes of eclampsia and stroke during pregnancy.	Cases of eclampsia and stroke during pregnancy	Response rate was 100%. There were 126 cases of eclampsia (0.04% of all deliveries) and 26 cases of stroke (0.008% of all deliveries) The 26 cases of stroke included: 8 intracerebral hemorrhages, 5 SAH, 3 Moyamoya diseases, 4 intracerebral infarctions, 2 cerebral venous thromboses, 2 posterior reversible leukoencephalopathy syndromes and other (n=2) There were 6 stroke deaths (2 cerebral hemorrhages, 3 subarachnoid hemorrhages and 1 cerebral venous thrombosis) Eclampsia episodes occurred during labour or during the postpartum period in 39.7% and 43.6% of cases, respectively. Strokes occurred antepartum or postpartum in 34.6% and 53.9% of cases, respectively. 6 patients suffered further strokes Data from 35 cases of eclampsia or intracerebral hemorrhages during pregnancy revealed that at the time of occurrence, mean SBP and DBP was 177.3 $\pm$ 27.7 mmHg and 106 $\pm$ mmHg, respectively. All 4 fatal cases involved SBP greater than 180 mmHg **Recommendations** ***I. Therapeutic strategies for eclampsia and stroke during pregnancy:*** In pregnant women with eclampsia and stroke, priority be given to emergent care including performing vital examination, maintaining respiration,

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					ensuring any required oxygen/intravenous drip infusions are provided, and monitoring of fetal heart rate ***II. Discriminating between eclampsia and stroke:*** Discriminating between eclampsia and stroke during labour can be achieved via neurological scales (i.e. National Institutes of Health Stroke Scale); When a stroke is detected, collaborative treatment with a neurosurgeon should be started as soon as possible; Rapid maternal transport to an intensive medical institution is necessary **III. Antihypertensive therapy:** In patients with blood pressure greater than 160/110 mmHg, the use of $MgSo_4$ to decrease the risk of convulsions and reduce their blood pressure to 140-159/90-109 mm Hg should be considered; It is necessary to reduce blood pressure in patients with hypertension of greater than 180/120 mm Hg; Possible treatment include Methyldopa, hydralazine, nifedipine, labetalol, and nicardipine; Hydralazine is not suitable for patients with active cerebral hemorrhaging
Crovetto et al. 2013 **Italy** **Narrative Review**	NA	12 studies, published between January 1990 and April 2013 that examined the relationship between preeclampsia and stroke.	Narrative review summarizing the available data with regard to incidence, diagnosis and management of stroke in eclampsia or pre-eclampsia	Frequency of pre-eclampsia among women with pregnancy-induced stroke	The proportion of women suffering stroke who had concomitant pre-eclampsia or eclampsia was 36% (95% CI: 33-39%) Pre-eclampsia and eclampsia represented two of the most important risk factors for stroke within the first two weeks of the puerperium. Hemorrhagic stroke emerged as the most common type of stroke associated with pre-eclampsia/ eclampsia, probably because of severe hypertension. In women with severe pre-eclampsia, the presence of headache, impaired consciousness and SBP should be evaluated as they are the most common symptoms of stroke in the context of pre-eclampsia/ eclampsia, and drugs focused on the treatment of hypertension and prophylaxis against seizures have to be started soon.

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					The prophylactic use of aspirin, started before 16 weeks of gestation may help to reduce the risk of pre-eclampsia in high-risk women. Aspirin is also an important prevention strategy for ischemic stroke in women; therefore, prevention with aspirin represents an important overlap between these two disorders.
Fischer-Betz et al. 2012 **Germany** **Prospective cohort**	NA	23 pregnancies in 20 women with primary (n=8) and secondary Antiphospholipid syndrome (APS) (n=12). Prior to pregnancy, 8 women had transient ischemic attacks (TIA) and 12 had strokes. Median age was 31 years. Median time from previous cerebrovascular event and pregnancy was 81 months.13 women had systemic lupus erythematosus; 5 had renal disease and 5 had HTN.	From the time pregnancy was detected, patients were evaluated regularly throughout their pregnancies until three months after delivery. All patients received aspirin 100 mg daily in combination with low molecular weight heparin during their pregnancies	Risk of pre-eclampsia Recurrence of cerebral ischaemic events (CVE)	There was a 3-fold increase of pre-eclampsia in women who were positive for multiple antiphospholipid antibodies (OR=3.06, 95% CI 1.01-9.32) per positive aPL test 3 women experienced recurrent CVE in the context of pregnancy (1 during pregnancy, 2 in the postpartum period) There was a non-significant trend of increased risk of new episode of CVE in patients with pregnancies complicated by pre-eclampsia. ***Recommendation:*** In the context of pre-eclampsia, anticoagulation should be given rigorously to prevent recurrence of CVE.
Tang et al. 2009 **Taiwan** **Population-based cohort study**	NA	1,132,019 live births occurring from 1996 to 2003.	Models were developed to estimate the effect of preeclampsia-eclampsia on the risk of hemorrhagic and ischemic stroke during pregnancy and within first postpartum year. Cases that had stroke before the index date were excluded, as were entries that represented extreme maternal age (≤15 or ≥50 years old), infant's birth weight (≤600	Hemorrhagic and ischemic stroke during pregnancy and within first postpartum year Analyses were adjusted for age, years of education, marital status, multiple gestation, birthweight, parity, anemia, diabetes, cesarean delivery, chronic hypertension, pregnancy-related hypertension, antepartum hemorrhage, and postpartum	Incidence of stroke was 21.47 cases per 100,00 deliveries (139 cases of hemorrhagic stroke and 107 cases of ischemic stroke) The risk of stroke at various time points given the presence of preeclampsia-eclampsia were: *Within 3 months antepartum:* Hemorrhagic stroke: RR=10.68, 95% CI 3.40- 33.59 Ischemic stroke: RR=40.86, 95% CI 12.14- 137.47 *Within first 3 days postpartum:* Hemorrhagic stroke: RR=6.45, 95% CI 1.42-29.29 Ischemic stroke: RR=37.71, 95% CI 11.08-108.68 *From days 3 to 6 weeks postpartum:* Hemorrhagic stroke: RR=11.76, 95% CI 4.05- 34.11

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			or ≥6000 gm), gestational weeks (≤19 or ≥45) and parity (≥11) [0.36%].	hemorrhage.	Ischemic stroke: RR=11.60, 95% CI 3.30- 40.82 *From 6 weeks to 6 months:* Hemorrhagic stroke: RR=11.76, 95% CI 4.05- 34.11 Ischemic stroke: RR= 11.60, 95% CI 3.30- 40.82 From 6 months to 12 months postpartum: Hemorrhagic stroke: RR=19.90, 95% CI: 7.75- 51.11 Ischemic stroke: RR=4.35, 95% CI 0.58- 32.92
Martin et al. 2005 **USA** **Retrospective study**	NA	28 women who suffered a pregnancy-associated stroke in association with severe preeclampsia and eclampsia from 1980-2009, at a single institution. Mean age was 30 years. Patients with other potential causes for development of stroke, such as a preexisting central nervous system lesion or a medical disorder like sickle hemoglobinopathy, were excluded.	Review of medical charts. Particular attention was paid to signs and symptoms recorded in the 6 –12 hour period immediately before and after stroke, including dipstick urinalysis for protein, weight, amount of edema (1– 4 +), and location, nausea and vomiting, epigastric pain, headache, change in sensorium, and eclamptic seizure. Laboratory findings obtained immediately before and immediately after stroke were accessed, when available	Blood pressure	12 strokes occurred in the antepartum period, 16 in the postpartum period Systolic BP in 24 patients recorded immediately before stroke was ≥ 155 mg Hg in 100% of women; while only 5 women (21%) had a diastolic BP ≥ 105 mm Hg Mean systolic and diastolic changes from pregnancy baseline to prestrike values were 64.4 mm Hg and 30.6 mm Hg, respectively Mortality rate was 53.6%. Permanent significant morbidity was reported in 89.3%. Headache, nausea and vomiting, epigastric or abdominal pain were the most commonly recorded symptoms prior to onset of stroke.
Ros et al. 2002 **Sweden** **Population-based cohort study**	NA	1,003,489 deliveries occurring from January 1, 1987 to September 30, 1995.	Information was collected at first antenatal visit and at the time of deliveries. The association between pre-natal complications and the risks of stroke and pulmonary embolus were estimated.	Pulmonary embolism and stroke Analysis was adjusted for age, parity, smoking, diabetes, and type of birth.	Preeclampsia was associated with a 3- to 12- fold increase of pulmonary embolism and stroke during late pregnancy, at delivery and in the puerperium. ***Pulmonary embolism:*** Third trimester: RR= 22.6, 95% CI 8.6-61.2 Delivery: RR= 211.7, 95% CI 52.4-856.3 Puerperium: RR= 79.8, 95% CI 41.9- 152.0 ***Stroke:*** Third trimester: RR= 18.3,95% CI 6.8- 49.5 Around delivery: RR- 669.7, 95% CI 328.9- 1363.4 Puerperium: RR= 39.9, 95% CI 17.6- 90.1

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
Lanska et al. 2000 **USA** **Retrospective cohort study**	NA	1,408,015 deliveries to women aged 18-44 years, during 1993-1994 occurring in 900 hospitals in 17 states.	Nationally-representative estimates of peripartum and postpartum stroke were calculated using data from the Healthcare Cost and Utilization Project, which representing 20% of hospitals nationwide. Models were developed to identify independent risk factors for stroke.	Stroke Intracranial venous thrombosis (IVT)	There were: 183 cases of peripartum stroke and 170 cases of peripartum IVT Estimated risks: 13.1 cases of peripartum stroke per 100,000 deliveries 11.6 cases of peripartum IVT per 100,000 deliveries Hypertension was a significant predictor of stroke: Peripartum: OR= 6.0, 95% CI 1.23-3.01 Postpartum: OR=2.24, 95% CI 1.37-4.2 Hypertension was a significant predictor of IVT: Peripartum: OR=1.93, 95% CI 1.23- 3.01 Postpartum: OR= 2.42; 95% CI 1.37-4.29. Types of hypertensive peripartum stroke patients (n=69) Essential hypertension (n=4) Renovascular hypertension (n=1) Gestational hypertension (n=7) Preeclampsia (n=36) Eclampsia (n=14) Eclampsia or preeclampsia superimposed on preexisting hypertension (n=7) Types of hypertensive peripartum IVT patients (n=23): Essential hypertension (n=2) Gestational hypertension (n=7) Preeclampsia (n=9) Eclampsia (n=1) Preeclampsia or eclampsia superimposed on preexisting hypertension (n=1) Unspecified hypertension (n=3) Peripartum stroke patients were more likely to have preeclampsia or eclampsia as reported cause of hypertension versus peripartum IVT patients (82.6% vs. 47.8%; OR: 5.2; 95% CI: 1.9, 14.5) Types of hypertensive postpartum stroke patient (n=36) Gestational hypertension (n=6)

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
					Preeclampsia (n=19) Eclampsia (n=9) Preeclampsia or eclampsia superimposed on preexisting hypertension (n=2) Types of hypertensive postpartum IVT patients (N=15): Essential hypertension (n=1) Gestational hypertension (n=5) Preeclampsia (n=5) Eclampsia (n=1) Unspecified hypertension (n=3) Postpartum stroke patients were more likely to have preeclampsia or eclampsia as the reported cause of hypertension versus postpartum IVT patients (83.3% vs. 40.0%; OR= 7.7, 95% CI 1.9- 29.1).

Treatment of Hypertension

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
Magee et al. 2015 **Canada** **RCT** ***Control of Hypertension In Pregnancy Study (CHIPS)***	CA: ☑ Blinding: Patient ☒ Assessor ☑ ITT: ☑	1,030 women from 111 centres in 16 countries, gestational age 14-33+6 weeks, with nonproteinuric, pre-existing or gestational hypertension (pre-existing hypertension: DBP ≥ 90 mmHg before pregnancy or 20 weeks' gestation; gestational hypertension:DBP ≥ 90 mmHg that developed> 20 weeks) and DBP of 90 - 105 mmHg if not taking antihypertensive therapy, or DBP of 85- 105 mmHg if taking antihypertensive	Women were randomized to 'tight' BP control (n=490) using antihypertensive agents, as necessary with a DBP goal of ≤85 mmHg vs. “less tight” (n=497) with a DBP goal of ≤ 100 mmHg, for the duration of their pregnancy. The recommended first-line agent was labetalol. ACE inhibitors, ARBs, direct renin inhibitors and atenolol were not permitted	**Primary outcome:** Composite of pregnancy loss or need for high-level neonatal care (>48 hours for 28 days or until discharge home) **Secondary outcome:** Serious maternal complications occurring up to 6 weeks postpartum (or until discharge, if longer), including death, stroke, eclampsia, blindness, uncontrolled HTN, use of inotropic agents, pulmonary edema, respiratory failure,	The median duration of study participation was 12.1 weeks. The frequency of the primary outcome was not significantly lower among women in the tight-control group (30.7% vs. 31.4%, adj OR=1.02, 95%CI 0.77-1.35). There were no significant differences between groups in the frequency of any of individual component of the primary outcome (miscarriage, ectopic pregnancy, elective termination, perinatal death, still birth or high-level neonatal care). The frequency of serious maternal complications was not significantly lower among women in the tight-control group (2.0% vs. 3.7%, adj OR=1.74, 95% CI 0.79-3.84).

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
		therapy. Women with severe systolic HTN were excluded. Mean age was 34 years. Mean weeks of gestation at randomization was 24.8. 75% of women had pre-existing HTN. 57% were taking antihypertensive agents at enrollment.		MI, hepatic dysfunction, hepatic hematoma or rupture, renal failure, and transfusion.	There was a single stroke/TIA in the tight-control group vs. 0 in the less-tight control group. The frequency of severe HTN was significantly higher among women in the less-tight control group (40.6% vs. 27.5%, adj OR=1.80, 95% CI 1.34-2.37).
Abalos et al. 2013 **South Africa** **Cochrane Review**	NA	48 RCTs (4,723 women) evaluating any antihypertensive drug treatment for mild to moderate hypertension during pregnancy. HTN was defined as SBP 140-169 mmHg and DBP 90-109 mmHg	RCTs comparing ≥1 antihypertensive drug vs. either placebo or no antihypertensive drug (n=29) and comparisons of one antihypertensive drug vs. another (n=22). Duration of treatment was at least 7 days. The antihypertensive drugs used in these trials included: alpha agonists (methyldopa), beta blockers (acebutolol, atenolol, labetalol, mepindolol, metoprolol, pindolol, oxprenolol and propranolol), calcium channel blockers (isradipine, nicardipine, nifedipine, nimodipine and verapamil), vasodilators (hydralazine and prazozin), ketanserin and glyceryl trinitrate.	**Primary outcome:** Severe HTN, proteinuria, any reported baby death, small-for-gestational age, preterm birth **Secondary outcomes:** Severe preeclampsia, eclampsia, HELLP syndrome,	**Any antihypertensive drug vs. none** The risk of severe HTN was significantly reduced in the active treatment group. RR= 0.49, 95% CI 0.40-0.60, p<0.0001. Results from 20 trials (2,558 women included. The risk of pre-eclampsia/proteinuria was not significantly reduced in the active treatment group. RR= 0.93, 95% CI 0.80-1.08, p=0.34. Results from 23 trials (2,851 women) included; however, in the sub group examination of beta blockers (vs. no treatment), the risk of developing proteinuria/pre-eclampsia was significantly reduced. RR=0.73, 95% CI 0.57-0.94. Results from 8 trials (883 women), included. The risk of fetal or neonatal death, pre-term birth or small-for-gestational age were not significantly reduced for women taking antihypertensive treatment **Any antihypertensive vs. methyldopa** The risk of severe HTN was significantly reduced with other antihypertensive agents, compared with methyldopa. RR= 0.54, 95% CI 0.30-0.95, p<0.0001. Results from 11 trials (638 women) included. The risk of proteinuria/eclampsia was significantly reduced with beta blockers or calcium channel blockers use compared with methyldopa. RR=0.73, 95%CI 0.54-0.99. Results from 11 trials (997 women) were included.

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
Nabhan & Elsedawy 2011 **Egypt** **Cochrane Review**	NA	2 RCTs (265 pregnant women) with mild or moderate pre-existing or non-proteinuric gestational hypertension. Mild HTN was defined as SBP of 140-159 mmHg and a DBP of 90- 99 mmHg; moderate HTN was defined as BPs of 160-169/100-109 mmHg, or as defined by study authors.	Women were randomized to tight vs. very tight control of mild-moderate, preexisting or non-proteinuric gestational hypertension. Antihypertensive agents used were methyldopa (n=1) and was labetalol (n=1). The target blood pressures were 100 mmHg for the less tight group and 85 mmHg for the tight group (n=1) and target BP of 130-139/80-89 mmHg vs. <130/80 mmHg (n=1).	**Primary outcome:** Severe pre-eclampsia, eclampsia, maternal death, perinatal deaths **Secondary outcomes:** Antenatal hospitalization, maternal admission to ICU, women's satisfaction, additional drugs to achieve control. Increase in dose of antihypertensive drugs to achieve control, gestational age at delivery, rate of induction of labor, rate of cesarean delivery, placental abruption, fetal distress, fetal growth restriction, birthweight, Apgar score <7 at one minute, admission to neonatal ICU.	The risk of any of the primary outcomes was not significantly increased in patients in the tight control group Severe preeclampsia: RR=1.28, 95% CI 0.97-1.70, p=0.08. Perinatal death: RR=1.48, 95% CI 0.25-8.74 There were no cases of eclampsia, maternal death or stroke The risk of all but one of the secondary outcomes was not significant increased among patients in the tight control group. More women in the tight control group were group were hospitalized during their pregnancy (RR= 2.53, 95% CI 1.14-5.63, p=0.023. The results from a single trial were included (n=125 participants)

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