ONTARIO MIDWIVES

EXPERTS IN NORMAL PREGNANCY, BIRTH & NEWBORN CARE

>Clinical Practice Guideline No.15

Hypertensive Disorders of Pregnancy

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Association of Ontario Midwives

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Hypertensive Disorders of Pregnancy (2012)

This document replaces ***AOM Clinical Practice Guideline No. 4 - Guideline for Monitoring Blood Pressure in Pregnancy.*** The original guideline was published in 2001.

This updated guideline was approved by the AOM board: April 4, 2012

Purpose

The goal is to provide an evidence-based clinical practice guideline (CPG) that is consistent with the midwifery philosophy and model of care. Midwives are encouraged to use this CPG as a tool in clinical decision-making. This CPG is independent of and not intended to replace the standards of the College of Midwives of Ontario.

Objective

The objective of this CPG is to provide a critical review of the research literature on the screening, diagnosis and management of hypertensive disorders of pregnancy (HDP) within the context of provision of midwifery care in Ontario. Evidence relating to the following will be discussed:

- Risk factors for HDP
- Prevention strategies for HDP
- Screening, diagnosis, assessment and monitoring of HDP
- Management of HDP in antenatal, intrapartum and postpartum care

Outcomes of Interest

1. Maternal Outcomes: incidence of HDPs; maternal morbidity; maternal mortality; rates of induction and caesarean section (CS)
2. Neonatal Outcomes: morbidity; mortality

Methods

A search of the Medline, CINAHL databases and Cochrane library from 1994-2010 was conducted using the key words: pregnancy, hypertension, preeclampsia, blood pressure. Additional search terms were used to provide more detail on individual topics as they related to HDP. Older studies were accessed in cases of commonly cited statistics, or significant impact on clinical practice.

Review

This CPG was reviewed using a modified version of the AGREE instrument (1), the AOM Values-based Approach to CPG Development (2), as well as consensus of the HDP Working Group, CPG Committee, the Insurance and Risk Management Program and the Board of Directors.

Abbreviations

Adj OR	Adjusted odds ratio	INR	International normalized ratio (prothrombin time)
ALT	Alanine aminotransferase (also known as SGPT)	IUGR	Intrauterine growth restriction
AST	Aspartate aminotransferase (also known as SGOT)	LDA	Low-dose aspirin
BMI	Body mass index (kg/m^2)	LDH	Lactate dehydrogenase
BP	Blood pressure (mmHg)	OR	Odds ratio
dBP	Diastolic blood pressure (mmHg)	PAPP-A	Pregnancy-associated plasma protein A
sBP	Systolic blood pressure (mmHg)	PROM	Prelabour rupture of membranes
CI	Confidence interval	PTT	Partial thromboplastin time
CS	Caesarean section	RCT	Randomized controlled trial
DIC	Disseminated intravascular coagulation	RR	Relative risk
HELLP	Hemolysis, elevated liver enzymes, low platelet count	SGA	Small for gestational age
HDP	Hypertensive disorders of pregnancy		

Key to Evidence Statements and Grading of Recommendations

The quality of evidence reported in this CPG has been assessed using the evaluation of evidence criteria recommended by the Canadian Task Force on Preventive Health Care.

Evaluation of evidence criteria		**Classification of recommendations criteria**	
I	Evidence obtained from at least one properly randomized controlled trial	A	There is good evidence to recommend the clinical preventive action
II-1	Evidence from well-designed controlled trials without randomization	B	There is fair evidence to recommend the clinical preventive action
II-2	Evidence from well-designed cohort (prospective or retrospective) or case-control studies, preferably from more than one centre or research group	C	The existing evidence is conflicting and does not allow to make a recommendation for or against use of the clinical preventive action; however, other factors may influence decision-making
II-3	Evidence obtained from comparisons between times or places with or without the intervention. Dramatic results in uncontrolled experiments (such as the results of treatment with penicillin in the 1940s) could also be included in this category	D	There is fair evidence to recommend against the clinical preventive action
III	Opinions of respected authorities, based on clinical experience, descriptive studies, or reports of expert committees	E	There is good evidence to recommend against the clinical preventive action
		L	There is insufficient evidence (in quantity or quality) to make a recommendation; however, other factors may influence decision-making

Reference: (3)

CONTENTS

BACKGROUND

Hypertensive disorders of pregnancy (HDP) are a major cause of poor pregnancy outcome in Canada and internationally. HDP encompasses a spectrum of conditions, including pre-existing hypertension, gestational hypertension and preeclampsia. These conditions range in severity from a mild increase in blood pressure at term with no additional signs, symptoms or adverse sequelae to multisystem conditions with the potential for significant maternal, fetal and neonatal harm. For many of the clinical manifestations of HDP, optimal strategies for prevention and management have yet to be determined, with delivery of the fetus being the only definitive treatment. (4) Despite extensive research, the onset of hypertension during pregnancy has proven difficult to predict. (5)

HYPERTENSIVE DISORDERS OF PREGNANCY

- Pre-existing hypertension
- Gestational hypertension
- Preeclampsia

Whether diagnosed before or during pregnancy, hypertension increases maternal risk of placental abruption, organ failure, cerebrovascular accident and disseminated intravascular coagulation (DIC), as well as fetal risk of intrauterine growth restriction (IUGR), intrauterine death and prematurity. (6) Despite these risks, mortality from HDP and serious morbidity are rare. While hypertension-related causes account for a large proportion of maternal deaths, absolute numbers remain low.

IMPLEMENTATION TIP

Practice groups may wish to create a written protocol specific to the practice group that documents which of the recommendations within the Clinical Practice Guideline they are adopting and how they are putting those recommendations into practice, including what would be part of an informed choice discussion with each client. Midwives are advised to clearly document that an informed choice discussion has taken place. If the practice group has a written protocol about what should be discussed with each client, that discussion should be followed. Any deviation from or addition to that discussion should also be documented in the woman's chart. If there is no protocol about what information is provided then documentation in the woman's chart should give details of that discussion. If, based on the client's health or risk status, the midwife makes recommendations for monitoring or intervention that the client declines, the midwife should document that her recommendation was declined.

Midwives monitor for elevated blood pressure and other signs and symptoms of HDP throughout the pregnancy, intrapartum and postpartum periods. Depending on its timing and severity, the condition may warrant consultation and/or transfer of care. (7) When care is shared with or transferred to a consultant, midwives may continue to provide management, monitoring, support and empathetic counselling to their clients and advocate on their behalf. As women who are diagnosed with HDP report increased levels of stress related to the diagnosis, particularly when they have HDP that is progressive and worsening, such support is especially vital. (8)

As Ontario midwives' scope of practice related to management of HDP is limited (see Table 1), readers are encouraged to look to other documents (particularly the CPGs produced by the Society of Obstetricians and Gynaecologists of Canada (SOGC) (9) and the National Institute for Health and Clinical Excellence (NICE) (10) for information concerning the management of HDP beyond the midwifery scope of practice.

Table 1: HDP and the Midwifery Scope of Practice

Depending on the timing and severity of maternal hypertension and the presence of proteinuria and/or adverse sequelae, the condition may warrant consultation and/or transfer of care under the College of Midwives of Ontario's (CMO) ***Indications for Mandatory Discussion, Consultation and Transfer of Care*** (IMDCTC).

Category 1	Discuss with another midwife or with a physician
Category 2	Consult with a physician
Category 3	Transfer to a physician for primary care

At initial history and physical examination	
History of essential or gestational hypertension	Category 1
History of gestational hypertension with proteinuria and adverse sequelae	Category 2
During prenatal care	
Hypertension arising during prenatal care	Category 2
Gestational hypertension	Category 2
Gestational hypertension with proteinuria and/or adverse sequelae	Category 3
Intrapartum	
Gestational hypertension	Category 2
Gestational hypertension with proteinuria and/or adverse sequelae	Category 3
Severe hypertension	Category 3
Postpartum	
Persistent hypertension	Category 2
Eclampsia	Category 3

Source: (7)

DEFINITIONS AND CLASSIFICATION

Historically, researchers and clinicians have used varied classification and definitions of HDP, making literature on this topic difficult to interpret. (11) The SOGC's Clinical Practice Guideline No. 206: ***Diagnosis, Evaluation and Management of Hypertensive Disorders of Pregnancy*** (2008) (9) uses a slightly different system of definition and classification from the British Columbia Reproductive Care Program's 2006 ***Guideline on Hypertension in Pregnancy*** (12), which is based on the definitions used in the Canadian Hypertension Society's 1997 guideline. (6) NICE (10), the ***Pre-eclampsia Community Guideline*** (PRECOG) (13) and the American Congress of Obstetricians and Gynecologists (ACOG) (14) use slightly different systems.

To enable clarity and communication in a multidisciplinary setting, this CPG encourages uniform use of terminology, classifications and definitions relevant to HDP. To that end, this CPG uses the definitions adopted by the SOGC in their most recent CPG on the ***Diagnosis, Evaluation and Management of the Hypertensive Disorders of Pregnancy***. (9) See Table 2 for a summary of previous and current classification systems.

Table 2: Comparison of HDP Classification Systems

Canadian Hypertension Society **BC Reproductive Care Program**	1997 2006	**Society of Obstetricians and Gynaecologists of Canada**	2008
A. Pre-existing hypertension (with or without proteinuria)		Pre-existing hypertension	
1. Essential			
2. Secondary		Pre-existing hypertension → with comorbid conditions	
B. Gestational hypertension		Gestational hypertension	
1. Without proteinuria			
a. Without adverse conditions			
b. With adverse conditions		Gestational hypertension → with preeclampsia	
2. With proteinuria			
a. Without adverse conditions			
b. With adverse conditions			
C. Pre-existing hypertension + superimposed gestational hypertension with proteinuria		Pre-existing hypertension with preeclampsia	
D. Unclassifiable antenatally		N/A	
Source: (6,12)		Source: (9)	

Definitions

The definition of **hypertension** in pregnancy is a diastolic blood pressure (dBP) of 90 mmHg or more, based on the average of at least two measurements taken using the same arm. (6,9,15) Repeat measurement should ideally occur on more than one visit, as research suggests that 30% to 70% of women with blood pressure (BP) ≥ 140/90 mmHg have normal BP on subsequent measurement. (9,16). No evidence was found to provide guidance on best practice related to the frequency of measurement of blood pressure in general or for reassessment of blood pressure to confirm non-severe hypertension. Guidance about timing of repeat measurement to diagnose hypertension is based on consensus-based practice and may be found on pages 27.

Severe hypertension is defined as a dBP of 110 mmHg or more or a systolic BP (sBP) of 160 mmHg or more. (6,9) Severe hypertension should be confirmed by repeat measurement in 15 minutes, using the same arm. (9)

Proteinuria is defined by a urinary protein measurement equal to or greater than 0.3 g/day in a 24-hour urine collection or ≥ 30 mg/mmol urinary creatinine in a spot urine sample. (9) See the sections titled "Assessment of Proteinuria" and "Detection of Proteinuria" (pages 23, 24) for a detailed explanation of equivalent measures of urinary protein.

Classification

Hypertensive disorders of pregnancy should be classified as pre-existing hypertension or gestational hypertension. **Pre-existing hypertension** predates pregnancy or is diagnosed before 20 weeks' gestational age (GA). **Gestational hypertension** is detected at or after 20 weeks' GA. (9)

For both pre-existing and gestational hypertension, two further subgroups are defined in the 2008 SOGC guideline: with comorbid conditions, or with preeclampsia (see Table 3). **Preeclampsia** is defined by the presence of hypertension ***and*** proteinuria ***or*** another of a series of signs and symptoms associated with end-organ dysfunction. In women with pre-existing hypertension, preeclampsia is defined by the presence of one of the following at or after 20 weeks' GA: resistant hypertension ***or*** new or worsening proteinuria ***or*** one or more other adverse conditions. In women with gestational hypertension, preeclampsia is defined as new-onset proteinuria ***or*** one or more of the other adverse conditions (see Table 3). **Severe preeclampsia** is defined as preeclampsia with onset before 34 weeks' GA, with heavy proteinuria (> 0.3-0.5 g/day by 24 hour urine collection) or with one or more adverse conditions. **Eclampsia** is defined by preeclampsia plus new onset of convulsions. (9)

A critical factor differentiating the SOGC definition of preeclampsia is that proteinuria is but ***one criterion*** for preeclampsia. Preeclampsia may be diagnosed in the absence of proteinuria, provided one or more other adverse conditions is present. Conversely, proteinuria is a ***requirement for diagnosis*** of preeclampsia in the definitions used by NICE, (17) PRECOG (13) and ACOG (14).

Table 3: Classification of the Hypertensive Disorders of Pregnancy: 2008 SOGC Guidelines

Source: (9)

Pre-existing hypertension	Diagnosis before pregnancy or prior to 20 weeks' GA	
Subgroups		
Pre-existing hypertension → with comorbid conditions	e.g. type 1 or 2 diabetes, renal disease, or another non-pregnancy related indication for anti-hypertensive therapy	
Pre-existing hypertension → with preeclampsia	One or both of:	• Resistant hypertension (requiring ≥ anti-hypertensive agents to control BP • New or worsening proteinuria • One or more adverse conditions*
	At or after 20 weeks' gestation	
Gestational Hypertension	Diagnosis at or after 20 weeks' GA	
Subgroups		
Gestational hypertension → with comorbid conditions	e.g. type 1 or 2 diabetes, renal disease, or another non-pregnancy related indication for anti-hypertensive therapy	
Gestational hypertension → with preeclampsia	One or both of:	• New proteinuria • One or more adverse conditions*

*Adverse conditions noted above:

- Maternal symptoms: persistent or new/unusual headache, visual disturbances, persistent abdominal or right upper quadrant pain, severe nausea or vomiting, chest pain or shortness of breath.
- Maternal signs of end-organ dysfunction: seizures, severe hypertension, pulmonary edema, or suspected placental abruption.
- Fetal morbidity: oligohydramnios, intrauterine growth restriction, absent or reversed end-diastolic flow in the umbilical artery by Doppler velocimetry, or intrauterine fetal death.
- Abnormal maternal laboratory testing:
  - elevated serum creatinine;
  - elevated AST, ALT or LDH with symptoms;
  - platelet count < 100 x 10^9/L; or
  - serum albumin < 20 g/L.

} According to local laboratory criteria - sample values below

Source:	NORMAL VALUES IN PREGNANCY *Pregnancy and Laboratory Studies: A Reference Table for Clinicians* (18)			NORMAL RANGE, ADULT FEMALE Gamma-Dynacare Medical Laboratories (19)	London Health Sciences Centre (20)
	First trimester	Second trimester	Third trimester		
Creatinine	35-62 µmol/L	35-71 µmol/L	35-80 µmol/	50-100 µmol/L	55-100 µmol/L
AST (SGOT)	3-23 U/L	3-33 U/L	4-32 U/L	< 31 U/L	< 32 U/L
ALT(SGPT)	3-30 U/L	2-33 U/L	2-25 U/L	< 36 U/L	≤ 33 U/L
LDH	78-433 U/L	80-447 U/L	82-524 U/L	110-215 U/L	< 214 U/L

SUMMARY: DEFINITION AND CLASSIFICATION OF HDP

To facilitate communication among a multidisciplinary health team, the definitions and classifications adopted by the SOGC in their 2008 Clinical Practice Guideline, Diagnosis, Evaluation and Management of the Hypertensive Disorders of Pregnancy should be used. (9)

Hypertension in pregnancy is defined as a dBP ≥ 90 mmHg, based on the average of at least two measurements taken using the same arm.

Severe hypertension is defined as a sBP ≥ 160 mmHg or a diastolic BP ≥ 110 mmHg.

Proteinuria is defined as a urinary protein measurement equal to or greater than 0.3g/day in a 24-hour urine collection or ≥ 30 mg/mmol urinary creatinine in a spot urine sample. Table 12 compares methods of measuring urinary protein.

Hypertensive disorders of pregnancy should be classified as pre-existing or gestational hypertension.

In women with pre-existing hypertension, **preeclampsia** is defined as resistant hypertension, new or worsening proteinuria, or one or more of the other adverse conditions noted in Table 3.

In women with gestational hypertension, **preeclampsia** is defined as new-onset proteinuria or one or more of the other adverse conditions noted in Table 3.

Severe preeclampsia is defined as preeclampsia with onset before 34 weeks' GA, with heavy proteinuria or with one or more adverse conditions noted in Table 3.

INCIDENCE OF HDP

Approximately 1% of pregnancies in Canada are affected by pre-existing hypertension, 5% to 6% by gestational hypertension without proteinuria, and 1% to 2% by preeclampsia. (9) Among women who gave birth in Ontario between April 2006 and March 2007, 0.7% of women had pre-existing chronic hypertension, 3.2% were diagnosed with gestational hypertension and 1.3% were diagnosed with preeclampsia. (21) Just over 12% of maternal deaths that occurred in Canada between 1999 and 2004 were attributed to hypertension complicating pregnancy, childbirth and the puerperium, corresponding to a cause-specific maternal mortality rate of 6 per 1 000 000 live births (95% confidence interval (CI) 3.4-10.3). (22) The incidence of HDP in Canada is similar to trends noted elsewhere. According to the World Health Organization (WHO), HDP accounts for 16% of maternal deaths in developed countries. (23)

It is anticipated that the incidence of HDP will rise with increasing population prevalence of obesity, chronic hypertension, diabetes and other predisposing conditions. (9) However, a recent decline in eclampsia has been noted:

between 2003 and 2009, incidence of eclampsia declined from 12.4 to 5.9 per 10 000 deliveries. This decline remained unchanged after adjustment for risk factors, leading the researchers to attribute the decline to improvements in the use of magnesium sulfate as a seizure prophylaxis. (24)

PHYSIOLOGY OF HDP

The etiology and pathophysiology of HDP remains unexplained. This may be due to the heterogeneous nature of HDP and its varied clinical progression. Pathogenesis may also differ according to the presence of risk factors and the timing of disease onset. (25) Despite extensive research, the causes of preeclampsia, in particular, are largely unknown.

Pathophysiology of Preeclampsia

Normal pregnancy is characterized by changes in blood pressure. In the first trimester, a decrease in blood pressure is caused by vasodilatation. By the second trimester a reduction in diastolic blood pressure by 15 mmHg is typical. (6) There is then a gradual increase in blood pressure until term, when pre-pregnancy levels are attained. (26)

Dominant hypotheses suggest the development of preeclampsia occurs in two stages. (27) The first stage of the disease process is thought to occur in early pregnancy, when typical physiological changes in the spiral arteries of the decidua and myometrium are inhibited, resulting in poor placental perfusion; early placental hypoxia and oxidative stress may also occur. In the second stage, poor placentation triggers the release of substances that damage the endothelial cells of the maternal circulatory system, provoking systemic inflammation and endothelial cell dysfunction, increasing vascular reactivity and leading to:

- Vasospasm and increased blood pressure;
- Abnormal coagulation and thrombosis;
- Increased endothelial permeability, resulting in proteinuria, edema and hypovolemia. (27)

Poor placentation can also cause fetoplacental demands to exceed maternal circulatory supply, restricting fetal growth and increasing the risk of stillbirth or neonatal death. (28) Fetal manifestations can occur before, with, or following maternal manifestations of preeclampsia. (9)

Current research suggests poor placentation is not a necessary cause of preeclampsia, but a powerful predisposing factor. In women in whom placental growth is appropriate for gestational age, or when preeclampsia has developed late in pregnancy, pre-existing cardiovascular or metabolic disorders may precipitate the cascade of systematic inflammation seen in the second stage of the disease process. (28) Maternal genetic, behavioural and environmental factors are thought to increase the risk of abnormal placentation and modify the progression of preeclampsia from stage one to stage two. (27)

Table 4: Likelihood that Gestational Hypertension will Progress to Preeclampsia

GA at diagnosis of new hypertension	Approximate rate of progression to preeclampsia	Source:
< 30 weeks	50%	(29)
< 34 weeks	35%	(9)
≥ 36 weeks	10%	(30)

Progression and Prognosis

In some cases, women who have been diagnosed with gestational hypertension will develop preeclampsia. The likelihood of progression decreases with GA at diagnosis (Table 4). Women with pre-existing hypertension experience a 10% to 20% risk of developing preeclampsia. (9)

Preeclampsia is a multisystem disease with variable progression. Maternal organ systems susceptible to the inflammation and endothelial damage of preeclampsia include the liver, kidneys, lungs and hematological and central nervous systems. Maternal and perinatal complications increase with the number of organ systems affected. See Table 5 for a description of ways in which preeclampsia may manifest.(28)

Table 5: Manifestations of Preeclampsia

Organ system involved	Pathological process	Sign/symptom
Central nervous system	Cerebral vasospasm and hemorrhage, ischemia and/or edema of the cerebral hemispheres	• Persistent headache • Visual disturbance • Seizure • Stroke • Clonus, hyperreflexivity • Hemiplegia
Hepatic system	Vasospasm and inflammatory infiltration	• Elevated liver enzymes • Falling albumin levels • Epigastric/right upper quadrant pain • Liver hematoma, rupture
Renal system	Damage to the endothelial cells of the glomerular capillaries as a result of vasospasm and decreased renal blood flow	• Proteinuria • Oliguria • Reduced creatinine clearance • Increased serum creatinine • Increased uric acid levels • Acute tubular necrosis
Respiratory system	Increased capillary permeability	• Dyspnea • Chest pain • Pulmonary edema • Cyanosis • Acute respiratory distress syndrome
Cardiovascular system	Vasospasm, increased capillary permeability	• Cardiomyopathy • Left ventricular failure • Pulmonary edema
Circulatory system	Peripheral vascular vasospasm and coagulation cascade activation	• Thrombocytopenia • Microangiopathic hemolysis • Low platelets • Prolonged prothrombin time • Low fibrinogen levels • Occluded blood flow to kidneys, liver, brain, placenta
Uteroplacental unit	Vasoconstriction reduces uterine blood flow	• Placental abruption • Placental scarring • Intrauterine growth restriction • Oligohydramnios

Based on: (12,31,32)

The majority of cases of preeclampsia in healthy primaparous women are mild and associated with little increased risk of adverse pregnancy outcome; approximately 75% are diagnosed near term or intrapartum. Frequency and severity of preeclampsia is higher in women with previous preeclampsia, multifetal pregnancies and pre-existing hypertension, diabetes mellitus and thrombophilias. (33) Research suggests that significant maternal morbidity arises in about 15% of women with severe preeclampsia. The tonic-clonic seizures of eclampsia are thought to occur in 1% to 2% of cases of severe preeclampsia. (28) Table 6 describes the incidence of complications of severe preeclampsia.

HELLP syndrome is characterized by hemolysis, elevated liver enzymes and low-platelet count; it is generally thought of as a variant form of preeclampsia, but can occur either with or without other typical symptoms of preeclampsia. (11) Serious maternal complications of HELLP syndrome include disseminated intravascular coagulation (DIC), placental abruption, and acute renal failure. (31)

Table 6: Complications of Severe Preeclampsia

Maternal complications	Observed incidence: women with severe preeclampsia
Placental abruption	1%-4%
DIC / HELLP syndrome	10%-20%
Pulmonary edema/aspiration	2%-5%
Acute renal failure	1%-5%
Eclampsia	~1%
Liver failure or hemorrhage	~1%
Stroke	Rare
Death	Rare
Fetal/neonatal complications	**Observed incidence: women with severe preeclampsia**
Preterm delivery	15%-67%
IUGR	10%-25%
Hypoxia/neurologic injury	~1%
Perinatal death	1%-2%

Source: (33)

FACTORS ASSOCIATED WITH THE DEVELOPMENT OF HYPERTENSION IN PREGNANCY

The highest volume and quality of research on the prediction of hypertension in pregnancy focuses on factors associated with preeclampsia.

Risk Factors for Preeclampsia

A 2005 systematic review of 52 cohort and case-control studies investigated risk factors for preeclampsia at first antenatal visit. A meta-analysis of the findings of the cohort studies included in the review suggested that presence of antiphospholipid antibodies, previous preeclampsia, pre-existing diabetes, multiple pregnancy, nulliparity, family history of preeclampsia, raised pre-pregnancy body mass index (BMI) and maternal age ≥ 40 were associated with an increased risk of preeclampsia. (34) Table 7 summarizes these findings. Table 7a explores the relationship between BMI and risk of preeclampsia in greater depth, suggesting that risk of preeclampsia rises with increasing BMI.

Other factors thought to increase risk of preeclampsia include paternal factors (including length of exposure to a single partner's sperm (35) and previous fathering of a preeclamptic pregnancy (36)), inter-pregnancy or inter-birth interval (37,38) and use of donor oocytes. (39,40) However, the mechanism, interrelationship, and/or strength of these associations is less well-established or consistent. (41-43) While young maternal age has also been invoked as a risk factor for the development of preeclampsia (9), the 2005 systematic review noted above did not find any association with increased risk of preeclampsia, regardless of age cut-off used. (34)

Table 7: Selected Risk Factors for Developing Preeclampsia

The table below lists risk factors identified in meta-analysis of cohort studies.

Risk factor No. of studies, no. of women	**Unadjusted pooled relative risk (95% CI)**
Past history	
Antiphospholipid antibodies* vs. none 2 studies, 1802 women	9.72 (4.34 – 21.75)
Previous preeclampsia vs. no previous preeclampsia 5 studies, 24 620 women	7.19 (5.85 – 8.83)
Pre-existing diabetes vs. none 5 studies, 56 986 women	3.56 (2.54 – 4.99)
Family history of preeclampsia vs. no family history of preeclampsia 2 studies, 692 women	2.90 (1.70 – 4.93)
Raised pre-pregnancy BMI vs. normal pre-pregnancy BMI** 6 studies, 64 789 women	2.47 (1.66 – 3.67)
Current pregnancy	
Twin pregnancy vs. singleton pregnancy 5 studies, 53 028 women	2.93 (2.04 – 4.21)
Primiparity vs. multiparity 3 studies, 37 988 women	2.91 (1.28 – 6.61)
sBP ≥130 mmHg at booking vs. sBP <130 mmHg at booking 1 study, 906 women	2.37 (1.78 – 3.15)
dBP ≥ 80 mmHg at booking vs. dBP <80 mmHg at booking 1 study, 907 women	1.38 (1.01 – 1.87)
Demographic factors	
Maternal age ≥ 40 vs. < 40 (primiparas) 1 study, 5242 women	1.68 (1.23-2.29)
Maternal age ≥ 40 vs. < 40 (multiparas) 1 study, 3140 women	1.96 (1.34-2.87)

*lupus anticoagulant and/or anticardiolipin
** Elevated BMI was defined variably in the studies included

Source: (34)

Table 7a: Association Between BMI and Preeclampsia

BMI	**Adjusted† odds ratio** (95% CI)
BMI 18.5-24.9	-
BMI ≥ 30	2.94 (2.87-3.01)
BMI 30-34.9	2.59 (2.52-2.66)
BMI 35-39.9	3.20 (3.09-3.32)
BMI 40-49.9	3.75 (3.59-3.92)
BMI ≥ 50	4.71 (4.20-5.28)

†Adjusted for maternal age, race, education level, parity, tobacco use, marital status, adequacy of prenatal care and presence of selected comorbidities (including anaemia, cardiac disease, insulin-dependent diabetes and other forms of diabetes, placenta previa and placental abruption and renal disease).

Source: (44)

Prediction and Prevention of HDP

Screening Tests for Early Prediction of Preeclampsia

Several clinical, biophysical and biochemical tests have been proposed as a means to predict preeclampsia, including serum alpha-fetoprotein, fetal fibronectin and uterine artery Doppler. A review of 27 different tests failed to identify a single biomarker or clinical factor that met the standards of clinical effectiveness typically applied to predictive tests. (45) Similar findings were noted in an earlier systematic review commissioned by the WHO. (5) The multicentre SCOPE trial's recent efforts to create a predictive model appropriate to primiparous women, based on presence of risk factors, met with only modest success. (46)

Researchers have noted an increased risk of HDP among women with abnormal maternal serum screening markers, including pregnancy-associated plasma protein-A (PAPP-A), placenta protein 13, inhibin-A and placental growth factor. (47,48) Among serum markers used in first trimester screening tests, PAPP-A appears to be the most strongly and/or consistently predictive of increased risk of HDP. (49-52) While PAPP-A measurement shows promise as a screening tool, its performance in clinical practice has not been established. Further research is required to test the clinical utility of PAPP-A measurement to predict risk of HDP and/or improve maternal or fetal outcomes. (53-55) In the meantime, low PAPP-A levels may warrant a higher index of suspicion for HDP.

Noting the heterogeneous nature of preeclampsia, researchers suggest that tests that combine information may be more effective than single biomarkers or clinical factors in predicting onset of the disease. Consequently, much current research on the prediction of preeclampsia involves the development of algorithms based on statistical models that incorporate findings from multiple tests. (56)

Preeclampsia Risk Stratification

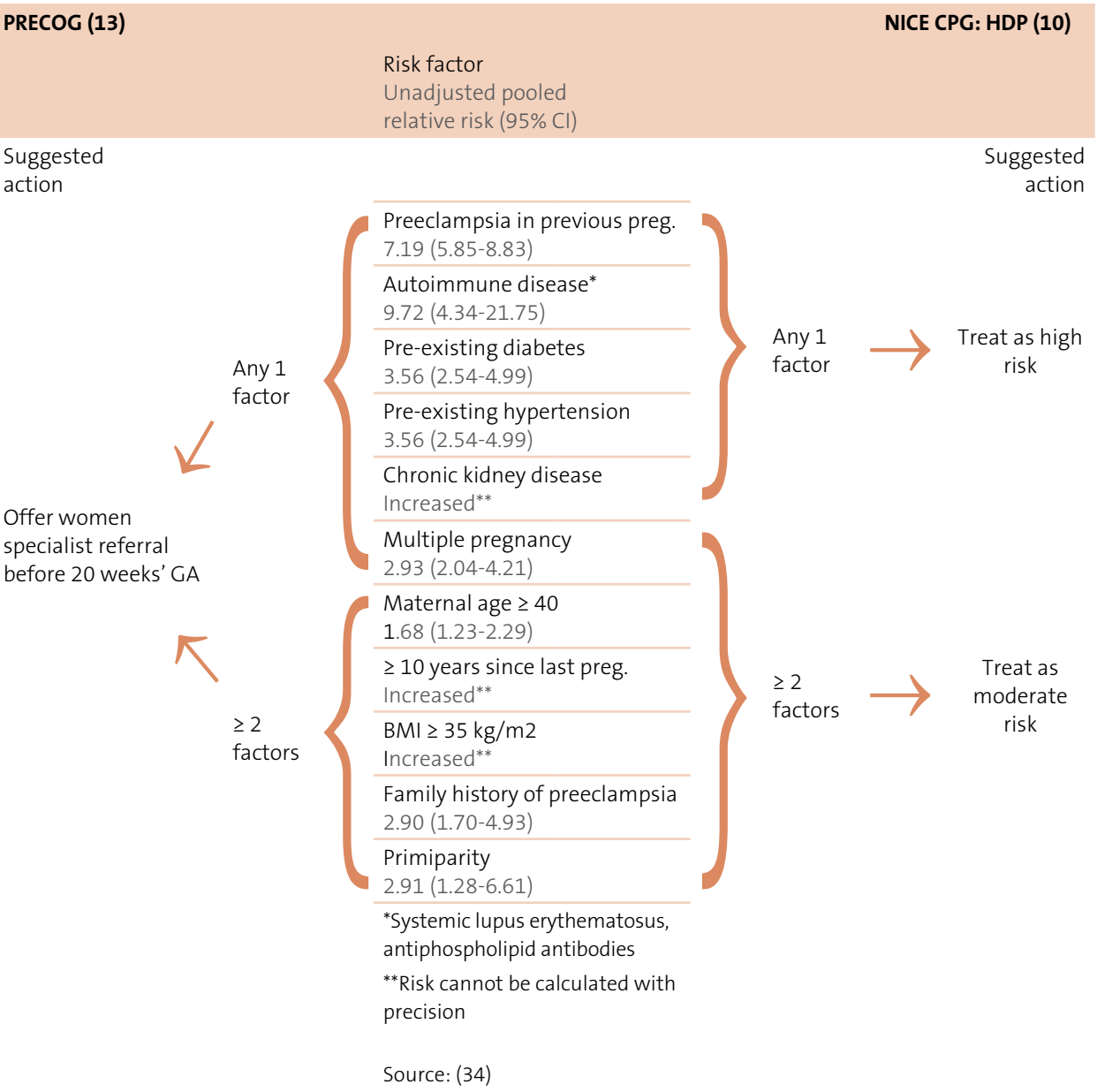
Researchers have attempted to integrate known risk factors for preeclampsia into risk stratification systems for use in routine antenatal care. The purpose of such systems is to identify women for whom additional monitoring and surveillance may be warranted. While risk stratification systems hold great intuitive appeal, there is little evidence at present to guide monitoring activities based on risk assessment, nor to substantiate their use in preventing adverse outcomes. Surveillance activities for women with suspected or established hypertension are better researched, and standardized protocols for antenatal and postpartum assessment and surveillance have been helpful in reducing maternal morbidity in high-risk settings (e.g. among women admitted to hospital with preeclampsia). (57)

The United Kingdom's PRECOG suggests categorizing clients according to their risk of developing preeclampsia based on predisposing factors ascertainable in early pregnancy. PRECOG also describes criteria for specialist referral according to the presence and timing of specified factors. (13) These criteria are not directly applicable to midwifery care in Ontario where the CMO specifies indications for referral. Nevertheless, midwives may find PRECOG useful in identifying women who may be at increased risk of preeclampsia, but do not yet meet the criteria described in the CMO's IMDCTC. (7)

The SOGC recommends risk stratification based on PRECOG's approach. The risk markers for preeclampsia noted in the SOGC CPG include risk factors identified in PRECOG as well as additional variables available later in pregnancy, or those for which the association with preeclampsia is weaker or less consistent. (9) NICE's CPG on routine antenatal care suggests increased monitoring in women who possess select risk factors. (15) See Table 8 for a comparison of two risk stratification systems.

While the risk factors included in risk stratification systems are largely substantiated by research evidence, their use in such systems is best characterized as consensus-based. In the absence of evidence to support appropriate and effective surveillance strategies, midwives can draw on existing risk stratification systems to inform discussions of risk within the wider context of a client's clinical picture. While a handful of relatively common demographic or pregnancy-related factors (e.g. primiparity, maternal age ≥ 40, maternal BMI ≥ 35) are associated with an increased risk of preeclampsia, most women who possess these risk factors will not be diagnosed with preeclampsia. Furthermore, the ultimate likelihood that preeclampsia will warrant significant intervention or result in major long-term harm is low. (28,33)

Table 8: Comparison of Risk Stratification Systems



RECOMMENDATIONS

1. Presence or absence of known risk factors for preeclampsia should be determined and communicated to clients early in care. Consultations should be arranged as indicated by the CMO's IMDCTC. (IIIA/B)
2. In the absence of consensus and clear evidence about what criteria should be considered in determining a woman's level of preeclampsia risk, midwives are encouraged to consider the client's clinical picture and consensus-based criteria in discussions related to client risk status and whether or not to undertake any potential preventive measures. (IIIB)

Prediction of Adverse Outcomes

Besides facilitating consistency and standardization of diagnosis, preeclampsia classification systems are intended to identify women and babies at increased risk of adverse outcomes. However, the severity criteria used by SOGC and ACOG have not been validated with respect to maternal or perinatal outcomes. A study assessing the severity levels used in the Canadian Hypertension Society's 1997 preeclampsia classification system suggested they were not predictive of maternal or perinatal morbidity. (57)

Preventative Measures

A substantial amount of research has also investigated the use of various prophylactic agents and behavioural modifications to reduce the incidence or severity of HDP.

Low-dose Aspirin

As preeclampsia is associated with activation of platelets and the maternal clotting system, researchers have hypothesized that antiplatelet agents, including low-dose aspirin (LDA), might either prevent or delay the development of preeclampsia or reduce its severity. This hypothesis has been tested in numerous studies. A 2007 Cochrane review included 59 randomized controlled trials (RCTs) of 37 560 women assessing LDA (50-150 mg/day) for the prevention of preeclampsia. LDA was associated with a 17% overall reduction in risk of preeclampsia (RR 0.83, 95% CI 0.77-0.89) and an 8% reduction in risk of birth before 37 weeks' GA (RR 0.92, 95% CI 0.76-0.98). Subgroup analysis assessed the effect of LDA in women who were considered to be at high risk of preeclampsia (due to presence of chronic hypertension, diabetes, kidney disease, autoimmune disorder or previous severe preeclampsia) and women considered to be at moderate risk of preeclampsia (including first pregnancy, mild elevation in BP, abnormal uterine artery Doppler velocimetry, elevated BMI, multiple pregnancy or family history of preeclampsia). Risk criteria varied among the studies included. Compared to placebo, LDA use was associated with a slightly greater reduction of risk of preeclampsia in women who were high risk (RR 0.75, 95% CI 0.66-0.85) than women who were moderate risk (RR 0.86, 95% CI 0.79-0.95). Among women considered high risk (criteria varied by study), only 19 (95% CI 13-34) would need to be treated to prevent one case of preeclampsia, whereas 119 (95% CI 73-333) women in the moderate risk group would need treatment to prevent one case of preeclampsia. Risk of gestational hypertension was reduced only among high risk women who took LDA (RR 0.54, 95% CI 0.41-0.70), though these findings were from small trials (838 women). No maternal or fetal harms were associated with prophylactic LDA use. (58)

Askie et al. used a different study design for a 2007 meta-analysis, aggregating individual data from over 30 000 women recruited to more than 30 RCTs. They concluded that LDA (50-150 mg/day) was associated with reductions in rates of preeclampsia (RR 0.90, 95% CI 0.85-0.97) and birth before 34 weeks' GA (RR 0.90, 95%CI 0.83-0.98). No particular subgroup of women was significantly more or less likely to benefit from LDA use. (59)

Based on available evidence, LDA may be consistent with a small to moderate reduction of risk of preeclampsia, especially in women at increased risk, and there appear to be no short- or long-term adverse outcomes associated with LDA use to prevent preeclampsia. Because studies have used different criteria to stratify women by risk level, authorities' recommendations about what populations of women should be offered LDA and at what dose are based

Table 9: Recommended Use of Low-dose Aspirin to Prevent Preeclampsia and its Complications: SOGC and NICE

	SOGC	NICE
Recommendation:	"Low-dose aspirin (75 – 100 mg/day) (III-B) should be administered at bedtime (I-B), starting pre-pregnancy from diagnosis of pregnancy but before 16 weeks' gestation (III-B), and continuing until delivery.(I-A)"	"...take 75 mg of aspirin daily from 12 weeks until the birth of the baby. "
Applies to:	"Women at increased risk"	"Women at high risk" or "women with more than one factor indicating moderate risk"
Source:	(9)	(10)

largely on clinical consensus. At present, the SOGC recommends LDA (75-100 mg/day) for women at increased risk of preeclampsia (see Table 9) starting before pregnancy or before 16 weeks' GA. (9) NICE recommends LDA use beginning at 12 weeks' GA, as it is the earliest gestational age for which research is available on the use of LDA to prevent preeclampsia. (10) While Askie's team found no difference in effect based on gestational age at which LDA was started (59), other researchers have found a greater risk reduction when LDA was started earlier in pregnancy. Bujold et al.'s meta-analysis of 27 studies (11 378 women) found a significant reduction in risk of preeclampsia (RR 0.47, 95% CI 0.34-0.65) among women who started LDA before 16 weeks' GA, and non-significant reduction in risk of preeclampsia among women who started LDA after 16 weeks' GA (RR 0.81, 95% CI 0.63-1.03). (60) There is no evidence to suggest an optimal gestational age at which to cease taking LDA. Both the SOGC and NICE recommend continuing LDA until delivery. (9,10)

Aspirin tablets are produced in standard sizes, which vary slightly by country. In the U.K., where much of the research on LDA has been published, a standard LDA tablet is 75 mg; this amount is considered to be clinically equivalent to the 81 mg tablet marketed as LDA in North America. In both cases, the low-dose equivalent is equal to one-quarter of the regular dose of aspirin (300 mg in the U.K., 325 mg in North America).

Informed choice discussions related to over-the-counter drugs should be documented in the same manner as prescribed drugs recommended or given by the midwife, with the dose, route and frequency recorded in the client's chart. (61)

Calcium Supplementation

Two recent reviews assessed the potential benefits of calcium supplementation during pregnancy to reduce the incidence of HDP. While the mechanism by which calcium levels influence blood pressure is not fully understood, it is hypothesized that calcium may reduce vasoconstriction and smooth muscle contractility. In a 2010 Cochrane review including 13 RCTs, calcium supplementation ≥ 1 g/day was associated with a reduced risk of hypertension compared to placebo (RR 0.65, 95% CI 0.53-0.81). Calcium supplementation was also associated with a reduction in the risk of preeclampsia (RR 0.45, 95% CI 0.31-0.65) and risk of preterm birth (RR 0.76, 95% CI 0.60-0.97). (62) The reduction in risk of hypertension or preeclampsia was most pronounced in women who were either at high risk of preeclampsia or had low baseline levels of dietary calcium (see Table 10).

Table 10: Calcium Supplementation ≥ 1 g/day and Risk of Gestational Hypertension and Preeclampsia

	Gestational hypertension	**Preeclampsia**
	Pooled relative risk (95% CI)	Pooled relative risk (95% CI)
All studies included in meta-analysis	0.65 (0.53-0.81) 15 470 women 12 studies	0.45 (0.31-0.65) 15 730 women 13 studies
Women at high risk* of developing preeclampsia	0.47 (0.22-0.97) 327 women 4 studies	0.22 (0.12-0.42) 587 women 5 studies
Women with adequate calcium diet	0.90 (0.81-0.99) 5022 women 4 studies	0.62 (0.32-1.20) 5022 women 4 studies
Women with low-calcium** diet	0.44 (0.28-0.70) 10 418 women 7 studies	0.36 (0.20-0.65) 10 678 women 8 studies

*"High risk" was variably defined in the studies included, and comprised adolescent women, women with previous preeclampsia or chronic hypertension, and women with increased sensitivity to angiotensin II.

** "low-calcium" diet was variably defined in the studies included

Source: (62)

While the accumulated evidence suggests that calcium supplementation may reduce the risk of preeclampsia, this effect seems to be most profound when dietary calcium intake is known to be low. "Low dietary calcium" was defined variably by the authors of the studies included in the Cochrane review, some of which were conducted in developing countries where overall caloric intake may be low and other nutrient deficiencies may be present. The relationship between calcium intake and preeclampsia is also thought to be influenced by preeclampsia risk status, though only small trials have been conducted among women considered to be at increased risk of preeclampsia (see Table 10). Calcium supplementation did not result in a statistically significant reduction in risk of either gestational hypertension or preeclampsia when calcium intake was known to be adequate. (62) While calcium supplementation has not historically been associated with any side effects or harms, the Cochrane review noted two trials (12,901 women) in which the risk of developing HELLP syndrome was higher for women who received calcium supplementation, rather than placebo (pooled RR 2.67, 95% CI 1.05-6.82). The authors suggested a possible explanation: calcium supplementation may have reduced blood pressure but not the underlying preeclamptic process, delaying diagnosis and treatment of preeclampsia and allowing more time for preeclampsia to progress to HELLP syndrome. (62)

For women with relatively varied, nutritious and energy-rich diets, calcium supplementation may not offer widespread benefit in terms of decreasing the risk of gestational hypertension or preeclampsia. Midwives may consider discussing the above findings with clients whose dietary calcium intake may fall below recommended levels or who have risk factors for developing hypertension. Health Canada suggests a recommended dietary allowance of 1000 mg of elemental calcium per day for women 19-50 years of age, including pregnant and breastfeeding women; tolerable upper intake levels are set at 2500 mg/day. (63) Women with calcium intake < 1000 mg/day may consider increasing their daily calcium intake to 1000 to 2500 mg/day by consuming additional foods high in calcium (i.e. dairy products or fortified soy beverages) or through supplementation.

Vitamin C and E

Oxidative stress is suspected to be one key factor contributing to the development of preeclampsia. Supplementation with antioxidants during pregnancy (such as vitamins C and E) has been proposed as a means of counteracting oxidative stress, thereby preventing or delaying the onset of preeclampsia. A 2008 Cochrane review of 10 RCTs (6553 women) found no significant difference between treatment and control groups for risk of preeclampsia (RR 0.73, 95% CI 0.51-1.06) or severe preeclampsia, preterm birth, small for gestational age (SGA) infants or neonatal death. (64)

A meta-analysis of nine RCTs (19 810 women) that assessed the combined effect of vitamins C (1000 mg/day) and E (400 mg/day) on various maternal and perinatal outcomes found no significant difference in risk of preeclampsia between vitamin and placebo groups (RR 1.00, 95% CI 0.92-1.09). Results were similar in a subgroup analysis of 13 525 nulliparous women at low to moderate risk of preeclampsia (RR 1.08, 95% CI 0.95-1.23). This review did note a significant increase in prelabour rupture of membranes (PROM) among women supplemented with vitamins C and E (RR 1.73, 95% CI 1.34-2.23) but a lower rate of placental abruption (RR 0.63, 95% CI 0.13-0.94). (65)

This meta-analysis includes a 2010 study conducted among 2363 women in Canada and Mexico. Vitamin C (1000 mg/day) and E (400 mg/day) supplementation did not reduce the rate of gestational hypertension or preeclampsia, compared to placebo, but did increase risk of PROM (RR 1.69. 95% CI 1.23-2.22) and preterm PROM (RR 1.97, 95% CI 1.31-2.98). This study also noted a higher rate of perinatal death (fetal death > 20 weeks GA or neonatal death within 7 days of birth) in the antioxidant group, compared to the placebo group, but the effect was not statistically significant (RR 5.12, 95% CI 0.60-43.79). When perinatal death was included in a composite measure of all fetal loss or perinatal death, the difference in risk was statistically significant (RR 2.20, 95% CI 1.02-4.73). The higher rate of fetal loss or perinatal death in the group receiving vitamin supplementation contribute to the data safety monitoring board's decision to end the trial early. (66)

High-quality evidence suggests vitamin C and E supplementation does not reduce the risk of preeclampsia or its complications. A limited body of research suggests antioxidant use may increase risk of PROM and preterm PROM, though the mechanism by which vitamin C and E supplementation may increase risk of early membrane rupture is unclear. (65) Further research is required to quantify this risk more precisely. In the meantime, the balance of suspected risks and benefits associated with vitamin C and E supplementation suggest it should not be recommended to reduce the risk of preeclampsia or its complications.

Supplementation with Fish Oil and Other Prostaglandin Precursors

Population studies have shown a relationship between high consumption of fish during pregnancy and low incidence of preeclampsia, suggesting that fatty acids contained in fish, which are precursors to prostaglandins and are known to modulate inflammatory and vascular effects, may contribute to this association. A Cochrane review of 6 RCTs (2755 women) evaluating the effect of supplementation with oils rich in omega-3 fatty acids found no significant difference in the relative risk (RR) of preeclampsia (RR 0.86, 95% CI 0.59-1.27) or hypertension (RR 1.09, 95% CI 0.90-1.33). (67) Four of the included studies used oil derived from fish, one used a mixture of evening primrose and fish oils, and the sixth used enriched eggs.

Micronutrient Supplementation

Deficiencies in pyridoxine (vitamin B6), zinc and magnesium have been hypothesized to increase the risk of HDP. Cochrane reviews have investigated the relationships between these micronutrients and maternal, fetal and neonatal outcomes, including outcomes associated with HDP and related complications.

A review of 5 RCTs comparing vitamin B6 administration in pregnancy with placebo found no statistically significant difference in the risk of eclampsia or preeclampsia. These trials were small (1646 women total) and of poor quality. (68)

A systematic review of zinc supplementation and maternal, fetal, neonatal and infant outcomes included 7 RCTs assessing the relationship between zinc supplementation (20-90 mg/day) and HDP. The authors found no significant difference in incidence of gestational hypertension or preeclampsia (RR 0.83, 95% CI 0.64-1.08). (69)

It has been suggested that magnesium supplementation may reduce growth restriction and preeclampsia. A review of randomized or quasi-randomized trials found only one study of high quality. This trial demonstrated no effect of magnesium supplementation on hypertension, preeclampsia or other pregnancy outcomes. (70)

The effect of folic acid supplementation on the development of preeclampsia has been assessed by two prospective cohort studies. (71,72) The more recent study, involving 2951 Ontario women recruited at 12 to 20 weeks' GA, found a reduced risk of preeclampsia (Adjusted OR (Adj OR) 0.37, 95% CI 0.18-0.75) with supplementation of multivitamins containing > 1 mg folic acid. No statistically significant reduction of risk was found with folic acid supplementation alone (Adj OR 0.46, 95% CI 0.16-1.31). (72) These findings were consistent with the prior study (1835 women), which found a reduction in risk of preeclampsia (OR 0.55, 95% CI 0.35-0.95) among women who took folic acid-containing multivitamins before 16 weeks' GA. (71) Further trials are needed to provide more definitive evidence of a relationship between folic acid and the development of preeclampsia, and to further elucidate the role played by other vitamins (e.g. vitamin B6) contained in multivitamin supplements.

Garlic

A Cochrane review identified one study (100 women) investigating the effectiveness of garlic in reducing risk of preeclampsia. There was no statistically significant difference in incidence of preeclampsia between the women supplemented with garlic tablets (800 mg/day) and placebo (RR 0.78, 95% CI 0.31-1.93). (73)

Exercise

Regular exercise has been proposed as a preventative strategy for HDP based on the well-established association between physical activity and reduced risk of hypertension in non-pregnant women. Possible explanations for such a relationship include enhanced vascularization and placental growth, reduced oxidative stress, and lowered inflammatory cytokines. A Cochrane review included two small trials, and found no significant relationship between exercise and risk of developing preeclampsia (RR 0.31, 95% CI 0.01-7.09). (74)

Rest

A survey of Canadian maternity care providers suggests rest or reduction of physical activity is frequently suggested as a means of preventing HDP. (75) However, there is little research to support these recommendations. A Cochrane review of two trials found a statistically significant reduction in risk of preeclampsia with 4 to 6 hours of rest per day (RR 0.05, 95% CI 0.00-0.83), but no significant relationship between rest and risk of gestational hypertension (RR 0.25, 95% CI 0.03-2.00). These trials were small and of uncertain quality, and did not report potential adverse effects of rest, nor women's views or perceptions of impact on quality of life. (76)

SUMMARY: PREDICTION AND PREVENTION OF HDP

Predictive Tests

At present, there is no single test that accurately predicts the development of preeclampsia. Research on tests that combine clinical and laboratory findings using multivariable models is ongoing.

Low-dose Aspirin

Daily use of LDA (81 mg) appears to reduce the risk of preeclampsia in women at increased risk of developing the condition. In a Cochrane review of studies comparing LDA and placebo, women considered to be at moderate or high risk of developing preeclampsia experienced a 14% and 25% reduction in risk respectively (RR 0.86, 95% CI 0.79-0.95 and RR 0.75, 95% CI 0.66-0.85). Among women considered high risk (criteria varied by study), only 19 (95% CI 13-34) would need to take daily LDA to prevent one case of preeclampsia, whereas 119 (95% CI 73-333) women in the moderate risk group would need to take LDA to prevent one case of preeclampsia. No difference in maternal or fetal morbidity was noted for women who took LDA at the recommended daily dose. Because studies have used different criteria to stratify study populations by risk level, it is not clear what women would benefit the most from daily LDA use. While LDA seems to have the greatest benefit when it is started before 16 weeks' GA, there is no evidence to suggest there are risks associated with starting LDA at a later gestational age.

Calcium

Calcium supplementation appears to reduce the risk of hypertension and/or preeclampsia, though this effect seems to be strongest in women whose dietary calcium intake is low and/or who are at increased risk of preeclampsia.

Vitamin C and E

High-quality evidence suggests vitamin C and E supplementation does not reduce the risk of preeclampsia or its complications. A limited body of research suggests antioxidant use may increase risk of PROM and preterm PROM. Until further research quantifies this risk more precisely, the balance of possible risks and benefits suggests that routine supplementation of vitamin C and E should not be recommended for the prevention of preeclampsia.

Nutritional/Micronutrient Supplementation

Current research does not suggest fish oil supplementation is effective in preventing HDP. There is insufficient evidence to recommend vitamin B6, zinc, magnesium, folic acid or garlic supplementation for the prevention of HDP.

Lifestyle Modification

There is insufficient evidence to make conclusions about the effects of exercise and/or rest on the prevention of HDP.

RECOMMENDATIONS

3. If consistent with community standards, offer low-dose aspirin (81 mg/day) to women at increased risk of developing preeclampsia, beginning once the client's increased risk has been identified (ideally before 16 weeks' GA), and continuing until delivery. (IA)

4. Inform women whose dietary calcium intake is below recommend levels (< 1000 mg/day) and women who are at increased risk of developing hypertension that calcium supplementation appears to reduce the risk of preeclampsia. Recommend increased calcium intake (1000-2500 mg/day) through calcium supplementation or by consuming additional servings of foods high in calcium (equivalent to 1000-2500 mg/day). (IA/B)

ANTENATAL CONSIDERATIONS

Screening and Detection

While standard antenatal care includes screening for elevated blood pressure at every antenatal visit and protein excretion is typically measured at the same time, the optimal frequency and timing of blood pressure measurement and the diagnostic value of screening for proteinuria has not been definitively established. A Cochrane review of trials in high-income countries comparing antenatal care schedules involving a reduced number of visits (8-12 over the antenatal period) with standard care (13-14 visits) found no clear difference in maternal or perinatal outcomes, including preeclampsia and gestational hypertension. (77)

Research suggests that conventional methods of screening are not especially useful for either identifying or ruling out HDP. More than 20% of women will receive a blood pressure reading of 140/90 mmHg or higher after 20 weeks' GA. Blood pressure will remain elevated, and other symptoms of preeclampsia will develop, in a minority of these women. (78) In one review, hypertension or proteinuria was absent in 12% to 18% of women with HELLP syndrome. (79) Given the varied clinical manifestations and unpredictable onset of HDP, opportunistic monitoring of blood pressure, protein excretion and other signs and symptoms is justifiable and advisable. The poor performance of current screening methods means unnecessary interventions will likely occur, and in rare cases HDP will develop and progress despite rigorous monitoring.

Measurement and Recording of Blood Pressure

Accurate and consistent assessment of BP requires the consideration of a number of factors. As anxiety, excitement, caffeine, or physical or emotional stress may cause transient elevations in BP, allow at least 5 minutes of rest before measuring. (9,80) The client should be seated, with her arm positioned at the level of the heart, as brachial artery pressure is highest when upright (and lower in a supine or lateral position). Consequently, a reading taken when a client is reclined may be falsely low. (6) A cuff at least 1.5 times the circumference of the client's arm should be used, as an undersized cuff may overestimate sBP by 7 to 13 mmHg and dBP by 5 to 10 mmHg. (9) Using an oversized cuff is thought to introduce less error than using an undersized cuff. (13)

BP can be measured using either a mercury sphygmomanometer or calibrated aneroid sphygmomanometer; aneroid devices should be recalibrated against a mercury device on a regular basis (the SOGC suggests every two years, while other authorities recommend annual or twice-yearly recalibration). (9,81,82) Automated blood pressure measurement devices are typically not calibrated for use during pregnancy and are thought to be particularly likely to underestimate blood pressure in pregnant women who are hypertensive. (6,9,83) Mercury sphygmomanometers (or calibrated aneroid devices) remain the blood pressure measurement device of choice among many guideline-developing authorities. (6,9,14,84),

sBP is determined by the onset of palpation or appearance of clear tapping sounds, or Korotkoff phase I. Korotkoff phase V (disappearance) should be used to denote dBP, as it is more consistently detected and measured than Korotkoff phase IV (muffling) (see Table 11). (85) The previous AOM CPG suggested midwives use both Korotkoff phase IV and V (e.g. 100/70/62) or just Korotkoff phase IV to denote dBP. This recommendation was based on a consensus opinion of the Canadian Hypertension Society. (6) At the time, there was little research on

the clinical outcomes correlated with either phase, and phase IV was thought to offer a wider margin of safety in identifying women at risk of HDP. (6) More recent opinion suggests similar pregnancy outcomes regardless of whether phase IV or V are used to record dBP. (86) Due to its greater reliability, Korotkoff phase V should be used to denote dBP, with use of phase IV (muffling) recommended only in cases where Korotkoff sounds are still audible as the level approaches 0 mmHg. (85)

Table 11: Korotkoff Sounds

Phase	Description
Phase I	Appearance of clear tapping sounds corresponding to the appearance of a palpable pulse
Phase II	Sounds become softer and longer
Phase III	Sounds become crisper and louder
Phase IV	Sounds become muffled and softer
Phase V	Sounds disappear completely

Source: (87)

Midwives should be mindful of "white coat hypertension," also known as isolated office hypertension, a temporary elevation in blood pressure as a result of stress or anxiety experienced in the clinic setting, which may occur in up to 30% of pregnant women. (88) White coat hypertension is defined as home BP of < 135/85 mmHg and office dBP of ≥ 90 mmHg. (9) A Cochrane review found no trials comparing ambulatory blood pressure measurement (using a 24-hr automated device) during pregnancy with standard blood pressure measurement in clinic, while noting that self-measurement at home would seem to have some theoretical advantages. (88) If white coat hypertension is suspected, midwives should consider conducting a repeat measurement in the client's home in order to rule out white coat hypertension.

Assessment of Proteinuria

Proteinuria occurs when hypertension-associated decreases in renal blood flow damage the endothelial cells of the glomerulus of the kidney, allowing plasma proteins to filter into the urine. Renal damage is also signaled by reduced creatinine clearance. (31)

The presence or absence of proteinuria has traditionally been a key consideration in the diagnosis and prognostication of HDP, with proteinuria a necessary criterion for the diagnosis of preeclampsia in classification systems adopted by some authorities. (6) The 2008 SOGC CPG employs an "inclusive" definition of preeclampsia: hypertension must be accompanied by new or worsening proteinuria or one or more adverse conditions reflective of fetal or maternal complications. (9) This is consistent with the emerging conceptualization of proteinuria as simply one aspect of the complex pathophysiology of preeclampsia. (89)

While previous research suggested that likelihood of adverse maternal or fetal outcomes increases with higher levels of urinary protein (90), a growing body of research suggests that amount of proteinuria is a poor predictor of either maternal or fetal/neonatal complications in women with preeclampsia. (91-93) Consequently, the utility of using proteinuria as a marker of severity of preeclampsia may be limited. Proteinuria is nonetheless a common maternal manifestation of preeclampsia and assessing the presence or absence of urinary protein is a key step in the detection and management of HDP.

Proteinuria may also present without an increase in blood pressure. Pregnant women with isolated proteinuria may be at increased risk of progressing to preeclampsia. (94,95) A small retrospective cohort study found that 19 (51%) of 37 women who exhibited new proteinuria in the absence of hypertension progressed to preeclampsia ($p = .002$). (96)

Detection of Proteinuria

There are several methods of testing for proteinuria, including urinary dipstick testing, spot urinary protein/creatinine ratio, and 2-hour, 12-hour and 24-hour urinalysis. Researchers have not yet identified a method that best predicts adverse maternal or perinatal complications.

Testing for urinary protein by dipstick testing of a single urine sample is typical in provision of community-based maternity care due to ease of use, low cost and avail-

ability of a rapid result. A dipstick reading of nil or trace is considered to be negative for urinary protein; a value of +1 to +4 on a urine dipstick is considered positive for urinary protein. Most research on urinary dipstick testing has assessed the ability of dipstick tests to match the quantification of urinary protein excreted over the course of a 24-hour period. The inaccuracy of dipstick analysis, compared with the detection of proteinuria by 24-hour urinalysis, has been well documented; in one comparison, spot dipstick testing had a positive predictive value of 64.9% and a negative predictive value of 75.2%. (97) Dipstick results are thought to be confounded by inter-observer error, diurnal variation in protein excretion and levels of maternal hydration. (78,97,98) A recent cohort study conducted in Canada, the United Kingdom and Australia suggests that dipstick analysis is as effective as 24-hour urine collection and spot urine protein/creatinine ratio in predicting adverse events in women with preeclampsia. (91)

While the 24-hour urine protein measurement has long been considered the gold standard for quantification of proteinuria, it is also cumbersome, inconvenient and frequently affected by inaccurate collection. In a study conducted in women with HDP in British Columbia, protein measurements based on 24-hour urine collection were judged to be inaccurate due to the incompleteness of samples in 13% to 68% of cases. (93) Furthermore, researchers have failed to agree on a cut-off level on 24-hour urinalysis that has proven to be useful in predicting adverse maternal or perinatal outcomes. (89,92) While urinary protein excretion ≥ 0.3 g/day is commonly used to define proteinuria, 0.5 g/day has been suggested as a more clinically meaningful threshold. (89,99) Despite these limitations, 24-hour urine collection remains the most definitive and universally accepted means of quantifying the presence of urinary protein. (9)

Testing of the protein/creatinine ratio in a random (spot) urine sample has been accepted for diagnosis by SOGC, NICE, and the International and Australasian pregnancy hypertension societies, with proteinuria defined as ≥ 30 mg/mmol urinary creatinine. One review suggested pooled sensitivity and specificity of 83.6% (95% CI 77.5-89.7%) and 76.3% (95% CI 72.6- 80.0%) respectively, using 24-hour urinalysis as the reference standard. (100)

Table 12: Detection of Proteinuria: Approximate Equivalencies

Approx. protein concentration	***Method of detection***		
	Urine dipstick (dipstick value)	**24-hour collection** (Volume of protein)	**Protein:creatinine ratio** (Volume of creatinine)
< 0.1 g/L	Nil		
0.1-0.2 g/L	Trace		
0.3 g/L		*Proteinuria*	
	+1	0.3-0.5 g/day	30 mg/mmol
1.0 g/L		*Heavy Proteinuria*	
	+2	0.5-1 g/day	

Based on: (99,101)

It is suspected that protein readings from dipstick analysis may also be contaminated by leucorrhea, blood or semen, although no research is available to substantiate this possibility. (31) Midwives may find that recommending the use of an obstetrical towelette prior to voiding may reduce contamination and aid in obtaining an accurate result. While research suggests that perineal cleansing is not useful in reducing bacterial contamination of urine samples, its value in reducing leucorrhea, blood or semen has not been investigated. (102-105)

Accuracy of dipstick self-testing of urine as been assessed in a single study of 212 women recruited while receiving routine care at an Australian antenatal clinic, who were then verbally instructed in urine collection and dipstick testing. Comparing women's and nurses' interpretations of the same dipstick result, the researchers found that women tended to over-estimate proteinuria. (106) These findings add support to the common midwifery practice of engaging clients in the interpretation of dipstick results, and suggest that midwives should double-check dipstick results if they are reported as positive.

Discussion: Proteinuria

A growing body of research suggests that presence of proteinuria, rather than amount, is associated with increased maternal and perinatal morbidity. (89) Urine dipstick testing offers clear practical advantages and remains an appropriate method of screening for proteinuria in clients managed by midwives. Nevertheless, 24-hour urinary protein excretion tests remain the gold standard for the definitive diagnosis of proteinuria, with spot protein/creatinine ratios being increasingly used for diagnostic purposes. (91) If urinary protein equivalent to ≥ 0.3 g/L is found using urine dipstick, a midwife may consider whether or not retesting at a later time by urine dipstick or to facilitate a laboratory investigation such as protein/creatinine ratio or 24-hour collection is warranted based on the client's overall clinical picture (presence of leucorrhea, dehydration etc.).

Assessment of Other Signs and Symptoms of Preeclampsia

The most common maternal manifestations of preeclampsia are hypertension and proteinuria. In some cases, preeclampsia may progress in the absence of hypertension or proteinuria. Over one-third of women in a British study of women with eclampsia experienced seizures before hypertension or proteinuria had been identified. (107) Consequently, midwives and clients should be vigilant for other signs and symptoms of end-organ dysfunction associated with preeclampsia (see text box below; Table 5 offers a fuller explanation of the pathological processes underlying maternal and fetal manifestations of preeclampsia). Presence of edema and weight gain should not be used in the assessment of HDP, as neither is predictive of the progression of HDP. (13) As assessing liver enzymes and other biochemical and hematologic markers of HDP has become an important part of diagnosis and assessment of HDP, consultants may suggest such tests be done by the midwife prior to or after consultation. Table 13 (page 28) lists tests commonly used to monitor maternal and fetal well-being in HDP.

SYMPTOMS OF PREECLAMPSIA

- Persistent headache
- Visual disturbances (blurring, flashing, dark spots in the field of vision)
- Epigastric pain/right upper quadrant pain
- Nausea and/or vomiting
- Chest pain/shortness of breath

Fetal manifestations of preeclampsia may precede, coincide with, or occur in the absence of maternal signs or symptoms of preeclampsia. The incidence of IUGR in preeclamptic pregnancies is estimated at 30%. (9) Midwives should consider preeclampsia as a differential diagnosis while evaluating clinical findings suggestive of SGA or IUGR. Ultrasound evaluation of growth and fetal well-being should be considered when HDP is suspected as part of preparation for consultation.

Education

During the prenatal period, clients should be informed of the symptoms of advanced preeclampsia and should be aware of how to contact their midwife in the rare event these symptoms arise. Documentation of this discussion is recommended.

SUMMARY: ASSESSMENT OF BP, PROTEINURIA AND OTHER SIGNS AND SYMPTOMS OF PREECLAMPSIA

Measuring and Recording BP

- Use a calibrated device and a cuff of appropriate size
- Ensure client is relaxed, with arm supported at heart level
- Determine sBP by the onset of palpation or appearance of clear tapping sounds (Korotkoff phase I)
- Measure dBP as the disappearance of sounds (Korotkoff phase V)
- Read blood pressure to the nearest 2 mmHg

Assessment of Proteinuria

The optimal frequency, ideal method and ultimate value of screening for urinary protein have not been established.

Current opinion suggests dipstick testing is an appropriate method of screening for preeclampsia in the midwifery setting. (9,10,91) A negative dipstick reading does not necessarily rule out proteinuria, and a positive urine dipstick reading, in the absence of new hypertension, is prone to false positives. Midwives should provide adequate education to clients about urine collection and urinalysis, including how to read urine dipsticks and what to do in the case of an elevated reading.

A urine dipstick value ≥ +1 is considered to be equivalent to ≥ 0.3 g/L (≥ 0.3 g/day by 24-hour urinalysis). For women who test positive for urinary protein upon dipstick analysis, and have confirmed hypertension, further assessment and consultation with a physician is appropriate.

Other Signs and Symptoms of Preeclampsia

It is important for clients to be vigilant for symptoms of preeclampsia and aware of the importance of contacting their on-call midwife should they develop. When discussing the signs and symptoms of preeclampsia, it is helpful to place their risk into perspective; some symptoms (such as headache) are non-specific and are likely benign. Nevertheless, it is important to ensure clients are comfortable identifying symptoms and communicating any concern that should arise.

RECOMMENDATIONS

5. Discuss signs and symptoms of preeclampsia during the prenatal period (see "Symptoms of Preeclampsia" above) and ensure that clients are aware of how to contact their midwife in the event these symptoms arise. (IIIA)

Recommended midwifery actions when elevated blood pressure is detected in the absence of proteinuria:

6. For non-severe hypertension (dBP < 110 mmHg), at least two serial BP measurements using the same arm should be recorded before a diagnosis of hypertension is made. (II-2B)

    a) **If dBP is ≥ 90 mmHg and < 110 mmHg and dipstick urine testing is negative for proteinuria**, blood pressure should be reassessed by repeat measurement. Midwives will use their judgment to determine an appropriate interval between measurements, based on the client's gestational age, risk factors and presence of other signs and/or symptoms of preeclampsia.
    b) Conducting the second reading in the home environment is recommended when possible to rule out white coat hypertension. (II-2B)
    c) If an automated BP measurement device has been used for the first measurement, perform the second reading using a mercury sphygmomanometer or an aneroid device. (II-2B)
    d) Urinary protein should also be reassessed by dipstick at the time of the second BP measurement. (IIIB)
    e) Two successive readings of a dBP of ≥ 90 mmHg require a medical consultation. (IIIA)

7. **If sBP is ≥ 140 mmHg and < 160 mmHg and dBP < 90 mmHg, and dipstick urine testing is negative for proteinuria**, assess whether the client has risk factors for transiently elevated sBP (e.g. stress, caffeine, recent exercise) and determine whether or not to reassess the client's BP within a shorter time interval based on the client's clinical picture, while advising the client to contact her midwife if any other signs and symptoms of preeclampsia develop in the meantime. As elevated sBP may be a precursor to the subsequent development of diastolic hypertension, a higher index of suspicion may be warranted for these clients. (IIIB)

8. **For severe hypertension (dBP ≥ 110 mmHg, sBP ≥ 160 mmHg), with or without proteinuria**, further investigation and/or prompt assessment in a hospital setting and consultation with an obstetrician is warranted (Category 3 IMDCTC). (IIIA)

Recommended midwifery actions when blood pressure is elevated and in the presence of proteinuria:

9. a) If dBP is ≥ 90 mmHg and < 110 mmHg and proteinuria (equivalent to ≥ 0.3 g/L or more or ≥ +1 on urine dipstick) is present, midwives should use their clinical judgment to determine whether or not a reassessment should occur at home or in hospital the same day to confirm hypertension and presence of proteinuria. (IIIB)
    b) **If hypertension and proteinuria are confirmed**, further investigation and/or medical consultation and transfer of care is warranted. (IIIA)

Recommended midwifery actions when urinary protein is elevated:

10. a) For urine dipstick values equivalent to ≥ 0.3 g/L (≥ +1 on urine dipstick) in addition to other signs or symptoms of preeclampsia, further investigation and/or a prompt medical consult should be arranged. (IIIA)
    b) **If a urine dipstick value equivalent to ≥ 0.3 g/L (≥ +1 on urine dipstick) is noted in the absence of elevated blood pressure or other signs and symptoms of preeclampsia**, repeat the dipstick urinalysis. Midwives will use their judgment to determine an appropriate interval between measurements, based on the client's gestational age and risk factors. Midwives may suggest that clients use an obstetric towelette before producing the second sample to reduce the likelihood of a false-positive result. If urine dipstick reading remains equivalent to ≥ 0.3 g/L, further investigation and/or a medical consult is indicated. (IIIC)

MANAGEMENT OF HDP

Treatment options for HDP vary according to diagnosis, severity, gestational age, the woman's wishes and the consultant's recommendations. The information provided below is intended to provide a brief overview of some possible management options for the care of women diagnosed with HDP. For women diagnosed with HDP, midwives may facilitate informed choice discussions, monitoring or provision of supportive care to their clients depending on the severity of the HDP and community standards. For further details regarding the management of HDP, midwives are encouraged to consult the SOGC's Clinical Practice Guideline No. 260: Diagnosis, Evaluation and Management of the Hypertensive Disorders of Pregnancy. (9)

Antepartum Management

Antepartum Surveillance of Women with Chronic or Gestational Hypertension

The goal of antepartum surveillance in women with chronic hypertension and gestational hypertension is to watch for exacerbation of hypertension and progression to preeclampsia. (108) Women with pre-existing hypertension experience a 10% to 20% risk of developing preeclampsia. For women with gestational hypertension, risk of progression to preeclampsia depends on gestational age at onset of hypertension; approximately 35% of women who are diagnosed with gestational hypertension prior to 34 weeks' GA will develop preeclampsia. (9) While there is consensus among obstetrical clinical guidelines that heightened maternal and fetal surveillance is warranted, the optimal methods and frequency of such activities are unknown. See Table 13 for a list of common methods of maternal and fetal surveillance in pregnancies complicated by HDP. (9,14,108)

Antepartum Surveillance of Women with Preeclampsia

The goal of antepartum surveillance in women with preeclampsia is to detect end-organ dysfunction. (108) While research suggests serial surveillance of maternal and fetal well-being in women with preeclampsia appears to improve maternal outcomes, the value of specific surveillance activities has yet to be established. (10) For instance, the ideal frequency with which blood pressure should be measured has not been studied.

In one Vancouver-based study, a twice-weekly regimen of testing blood pressure and hematologic, renal, hepatic, and respiratory function, along with fetal surveillance, reduced incidence of adverse maternal outcome from 5.1% to 0.7% (OR 0.14, 95% CI 0.04-0.49) in a cohort of women admitted to hospital with preeclampsia. This standardized surveillance regimen had no impact on fetal outcomes. (109)

According to a survey conducted among Canadian physicians in 1999, more than 80% of obstetricians assessed complete blood count, coagulation, serum creatinine and uric acid, and alanine aminotransferase (ALT), aspartate aminotransferase (AST), and lactate dehydrogenase (LDH) at least once per week in women with preeclampsia. (110) Proteinuria (by dipstick and/or 24-hour urinary protein) was another biomarker frequently assessed by Canadian physicians, (110) though a growing body of research suggests that measurement of proteinuria is a poor predictor of either maternal or fetal/neonatal complications in women with preeclampsia. (89,91-93)

Table 13: Common Methods of Monitoring Maternal and Fetal Well-being in the Presence of Hypertensive Disorders of Pregnancy

MATERNAL		FETAL
• Hemoglobin	• Glucose	• Fetal movement count
• Platelet count	• AST	• Non-stress test
• Leukocytes and differential	• ALT	• Biophysical profile
• INR and PTT	• LDH	• Deepest amniotic fluid pocket
• Fibrinogen	• Albumin	• Fetal growth by ultrasonography
• Serum creatinine	• Bilirubin	• Umbilial artery Doppler
• Serum uric acid		

Adapted from: (9)

Antihypertensive Therapy

There is a general consensus that antihypertensive treatment decreases morbidity and mortality in pregnant women with severe hypertension, though it is not clear which antihypertensive agents are most effective. (10,28,111,112) The value of antihypertensive therapy for treating mild to moderate hypertension is less clear. A Cochrane review included 28 RCTs (2409 women) comparing antihypertensive drugs and placebo. While use of antihypertensive drugs was found to reduce the risk of progression to severe hypertension by half (RR 0.50, 95% CI 0.41-0.61), it had no significant effect on risk of preeclampsia (RR 0.97, 95% CI 0.83- 1.13) nor any neonatal outcomes assessed. (113)

While magnesium sulfate is no longer considered to be a useful first-line antihypertensive agent (9,28), there is strong evidence to recommend its use as an anticonvulsant. (12,111,112,114)

Induction of Labour

Antenatal management of pregnancies complicated by gestational hypertension and/or preeclampsia may involve weighing the benefits and risks of expedited delivery. While active management (via induction of labour) has the potential to prevent maternal complications associated with gestational hypertension and/or preeclampsia, induction of labour may increase perinatal morbidity and mortality, especially when hypertensive disorders develop remote from term, and increase the risk of CS. Current research does not permit straightforward conclusions about the circumstances to which active or expectant management strategies are best suited. (28,115)

According to a recent meta-analysis of data from RCTs and cohort studies, expectant management of severe preeclampsia presenting prior to 34 weeks' GA is associated with longer pregnancies (by 7-14 days) and improved neonatal outcomes compared to preeclamptic pregnancies managed actively, with few serious maternal complications. However, few of the studies included in this review directly compared expectant versus active management strategies. (116) Another recent review concurred that expectant management may be advantageous in some cases of severe preeclampsia < 34 weeks' GA, but identified persistent symptoms of severe preeclampsia, uncontrollable severe hypertension, eclampsia, pulmonary edema, placental abruption, disseminated intravascular coagulation, significant renal dysfunction, and abnormal fetal surveillance results as factors that may warrant expedited delivery. (117)

There is little research on optimal timing of birth in women who have mild or moderate hypertension and/or preeclampsia between 34 and 37 weeks' GA. (10,117) While induction mitigates the risk that mild or moderate disease will progress to severe hypertension and/or preeclampsia, it is not clear whether those benefits outweigh the increasingly well-established risks of short- and long-term morbidity associated with late preterm birth (34-36+6 weeks' GA). (118) A study assessing neonatal outcomes in women with mild gestational hypertension who were induced at 34 to 36+6 weeks' GA and women who were induced > 37 weeks' GA, found higher rates of CS, NICU admission, assisted ventilation and respiratory distress syndrome in late-preterm infants. (119)

The findings of the 2009 Dutch HYPITAT RCT suggest that after 37 weeks' GA, induction of labour is associated with improved maternal outcomes in women who have gestational hypertension or mild preeclampsia. The 377 women randomized to the induction of labour group delivered at a mean GA of 38.7 weeks. Almost half of the 379 women randomized to expectant monitoring ultimately underwent induction, mostly due to worsening disease, and delivered at a mean GA of 39.9 weeks. Progression to severe disease (severe hypertension, severe proteinuria, HELLP syndrome, eclampsia, lung edema, severe postpartum hemorrhage (≥ 1000 mL), or thromboembolic disease) occurred in 23% of the induction group and 36% of the expectant management group, corresponding to a relative risk of 0.64 (95% CI 0.51-0.80), an absolute risk reduction of 13% among the induction group, and a number needed to treat of 8.

One concern with this trial is that a composite measure was used to indicate poor maternal outcome. Progression to severe hypertension (sBP ≥ 170 or dBP ≥ 110) and postpartum hemorrhage (≥ 1000 mL) reached statistical significance and comprised the majority of the morbidity experienced in both groups. Progression to severe sBP and dBP (measured on a single occasion) for the induction group was reduced by 8.63% and 10.73%, respectively. When severe sBP and dBP was defined based on 2 measurements, the absolute risk reduction dropped to 4.71% and 5.77%. There was not a statistically significant absolute risk reduction for PPH among groups, nor in maternal stay in intensive care units or any other measurment included in the composite. There was no difference in rates of CS or operative delivery between the two groups, nor any difference in any of the neonatal out-

comes assessed: fetal death, Apgar score < 7 at 5 minutes, arterial pH < 7.05, or admission to NICU. (120) The small size of the HYPITAT trial limits the conclusiveness of findings related to neonatal morbidity and mortality. Questionnaires completed by the women who participated in the HYPITAT trial at 6 weeks and 6 months postpartum found no difference in health-related quality of life between the induction and expectant management groups. (121)

While the HYPITAT trial involved only a small number of women, it is one of the few high-quality studies designed to explore management options available to women with HDP at term, and its findings have been cautiously embraced. (122,123) Based on the HYPITAT trial, NICE recommends birth within 24 to 48 hours for women with mild or moderate hypertension and preeclampsia after 37+0 weeks' GA. (10) It is not clear whether the low rate of CS observed in the HYPITAT trial (14% in the induction group and 19% in the expectant management group) could be reproduced in other settings. Approximately 27% of births that occurred in Ontario in 2004-2005 were by CS. (22) Higher rates of CS (particularly in association with induction of labour) could limit the external validity of the HYPITAT study's findings.

Intrapartum Management of HDP

HDP and Epidural Use

There has been debate about the use of regional anesthesia in women with HDP related to concerns about maternal circulatory volume, coagulopathy and blood pressure changes associated with epidural use. However, accumulated evidence does not suggest that epidural anaesthesia has different effects in women with HDP, compared to the general obstetric population. (10) Risk of hypotension associated with neuraxial anaesthesia is not increased in women with preeclampsia. (124) While studies have not been conducted among women with HDP, preloading with a bolus of crystalloid fluid does not appear to prevent hypotension in normotensive women. (9,12) Given the potential increase in risk of pulmonary edema with excess intravenous fluid intake, the SOGC recommends against preloading prior to administering regional analgesia and/or anaesthesia in women with HDP. (9) NICE also cautions against preloading fluids for women who have severe preeclampsia. (10)

Hospitals may have policies concerning the use of anaesthesia in women with HDP (for example, the SOGC recommends platelet counts for all women with HDP upon admission to the delivery suite and notes that some anaesthesiology departments may require tests of coagulation). (9) Midwives are encouraged to be familiar with policies in place at the hospitals at which they have privileges, even when such policies may be specific to the provision of care by other maternity care providers, and to consult with anaesthesia staff according to hospital policy.

Management of the Third Stage of Labour

Women with HDP are at risk of coagulopathy and thrombocytopenia. Consequently, the likelihood of postpartum hemorrhage may be increased. Active management of the third stage of labour for women with HDP is recommended. Ergometrine (ergonovine maleate) used prophylactically in the third stage of labour is associated with increased risk of elevated blood pressure (RR 2.60, 95% CI 1.03-6.57) and therefore should not be used as prophylaxis in women with HDP. (9,10,125)

SUMMARY: ANTEPARTUM AND INTRAPARTUM CONSIDERATIONS

While there is consensus that heightened maternal and fetal surveillance is warranted in women with HDP, the optimal content and frequency of such activities has yet to be determined.

Antihypertensive therapy may be recommended with severe preeclampsia, severe hypertension, or non-severe hypertension with comorbidities. The value of antihypertensive therapy for treating mild to moderate hypertension is less clear.

There is little research on optimal timing of birth in women who have mild or moderate hypertension and/or preeclampsia between 34 and 37 weeks' GA. The HYPITAT trial, while small, suggested improved maternal outcomes with induction of labour at 37 weeks' GA in women with gestational hypertension or mild preec-

lampsia. Current research does not permit straightforward conclusions about the circumstances to which early induction of labour or expectant management strategies are best suited.

Provided it is not contraindicated, epidural analgesia is appropriate in women with HDP.

Given the increased risk of coagulopathy and thrombocytopenia in women with HDP, active management of the third stage of is recommended. As ergometrine (ergonovine maleate) is associated with increased risk of elevated blood pressure, oxytocin should be used as prophylaxis for active management of the third stage.

RECOMMENDATIONS

11. Active management of the third stage of labour with oxytocin is recommended and should be offered to women with HDP. (IA)
12. Ergonovine maleate should be avoided in the prevention and treatment of PPH in women with HDP if other suitable uterotonic drugs are available. (II-3D)

Postpartum Considerations

HDP may resolve immediately following delivery, or can persist for several weeks or months postpartum. Hypertension and/or preeclampsia can also arise for the first time (***de novo***) in the postpartum period after a normotensive pregnancy. Similar to its antepartum manifestation, postpartum hypertension varies in its symptoms, signs and severity and the incidence, natural progression and optimal management of postpartum hypertension is not well understood. (126,127)

BP is thought to peak at 3 to 6 days postpartum, as extracellular fluid accumulated during pregnancy begins to mobilize, increasing intravascular volume and producing hypertension. These effects may be exacerbated by intravenous fluids administered during labour and delivery as well as the vasoconstrictive effects of medications used for pain relief or uterine atony. (127) Pre-pregnancy or gestational hypertension (with or without preeclampsia) and/or proteinuria may worsen at this stage, or new hypertension may arise. In a retrospective cohort study of 152 women readmitted to hospital with preeclampsia between 2 days and 6 weeks postpartum, a mean of 7 to 8 days elapsed between delivery and readmission. Almost two-thirds of these women had not been diagnosed with a hypertensive disorder prior to or during pregnancy. (128)

Clients should be informed that signs and symptoms of advanced preeclampsia (page 25) may occur during the postpartum period and should be made aware of how to contact their midwife in the rare event these symptoms arise.

Management of Postpartum Hypertension and Preeclampsia

Options for evaluation and management of postpartum hypertension or preeclampsia vary according to diagnosis, severity, laboratory findings and response to treatment. Postpartum hypertension or preeclampsia may occur secondary to a number of medical disorders (including thrombocytopenia and hemolytic uremic syndrome, pre-existing renal disease, pheochromocytoma and renal artery stenosis), and many of the signs and symptoms of postpartum hypertension or preeclampsia are non-specific. (127)

A Cochrane review of 6 trials of treatment of postpartum hypertension concluded that there is insufficient data to make recommendations about the use of antihypertensives in the postpartum period. (129) There is general consensus that severe hypertension (with or without preeclampsia) ought to be treated, and a wide range of antihypertensive agents are considered to be acceptable for use while breastfeeding. (9,127)

There is little generalizable data regarding the length of time to resolution of hypertension in women who developed hypertension while pregnant. In one older ob-

servational study, hypertension took longer to resolve in women with preeclampsia (a mean of 16 days) than in women with gestational hypertension (a mean of 6 days). (130) A study conducted among preeclamptic women in the Netherlands suggested that resolution time increased with severity of disease (as determined by maximal BP) and time between diagnosis and delivery. By 3 months postpartum, 61% of the women in the study were normotensive. (131)

In light of these findings, women who have had a HDP should be monitored closely in the postpartum period. Measure blood pressure at all regularly scheduled postpartum visits for the first 2 weeks postpartum or until blood pressure has returned to normal for 2 consecutive visits. Midwives should ensure clients are able to contact them if signs and symptoms of preeclampsia occur in the postpartum period. For women in whom blood pressure remains elevated, or continues to rise, more frequent monitoring should occur by scheduling additional postpartum visits and/or arranging a consultation with a physician depending on the client's overall clinical picture.

Postpartum Pain Management

The vasoconstrictive effects of medications frequently recommended by midwives for postpartum pain relief, such as nonsteroidal anti-inflammatory drugs (NSAIDs), may exacerbate postpartum hypertension. Case reports have attributed development of postpartum hypertension to NSAID use in the postpartum period. (132) Furthermore, side effects associated with NSAIDs (including elevated blood pressure, nausea, vomiting and headache) are similar to those of hypertension or preeclampsia. The mechanism by which NSAIDs increase blood pressure is unknown. Careful use of NSAIDs for management of postpartum pain, including ibuprofen, naproxen and diclofenac is warranted in women with HDP. A Cochrane review evaluating use of acetaminophen for the relief of postpartum perineal pain concluded that 500 to 1000 mg acetaminophen was generally effective for reducing pain, though studies tended to be old, of low quality and provided only limited information about side effects. The review's authors recommend further research to clarify any risks. (133) Reviews comparing acetaminophen to other forms of postpartum pain relief are underway.

Breastfeeding

Breastfeeding in women with HDP has not been well studied. A retrospective cohort study conducted in Germany concluded that women with HDP were less likely to initiate breastfeeding (RR 0.87, 95% CI 0.78-0.97) than normotensive women, and less likely to breastfeed at one month postpartum (RR 0.80, 95% CI 0.69-0.93). No difference between groups was found at 3 months postpartum. Authors attributed decreased likelihood of breastfeeding to increased rates of prematurity in the HDP group. (134)

Postpartum use of antihypertensives may be an additional consideration for breastfeeding women. Although an accurate estimation of drug passage into breast milk is difficult to estimate, many antihypertensive agents used in routine practice are considered safe for use during breastfeeding. (9,10)

Long-term Considerations

Women who develop gestational hypertension or preeclampsia may be at increased risk of hypertension and its cardiovascular implications in later life. Two large reviews suggest women who develop preeclampsia experience an increased lifetime risk of hypertension, cerebrovascular and cardiovascular morbidity and mortality, renal disease and thromboembolism. In both reviews, risk increased along with markers of disease severity. (135,136) The long-term risks of gestational hypertension are less established.

Due to potential increased risk of hypertension and cardiovascular disease later in life for women who have had HDP, these women may benefit from dietary and lifestyle changes. The postpartum period is an opportunity for midwives to discuss these risks and how healthy lifestyle choices (such as incorporating daily exercise and limiting total and saturated fat, cholesterol and sodium intake) may help to mitigate development of hypertension in later life. In addition, midwives should provide information about blood pressure issues that have arisen during the perinatal period to the care provider/family physician who will be providing ongoing care.

Future Pregnancies

It is important to share information with women about risk of HDP developing in subsequent pregnancies. Data from 5 cohort studies suggests that women who have had gestational hypertension have a 32% risk of developing gestational hypertension and 3% chance of developing preeclampsia in a subsequent pregnancy. Women with preeclampsia in previous pregnancy have a 38.5% risk of developing gestational hypertension and a 14.5%

chance of developing preeclampsia in a subsequent pregnancy (based on 8 retrospective cohort studies). For women who have had preeclampsia in a previous pregnancy, the more severe and earlier the onset in the index pregnancy the greater likelihood of development in subsequent pregnancies. (10)

SUMMARY: POSTPARTUM AND LONG-TERM CONSIDERATIONS

Antihypertensive therapy may be recommended with severe postpartum preeclampsia, severe postpartum hypertension, or non-severe hypertension with comorbidities.

Case reports on NSAID used to manage postpartum pain for women with HDP suggest that use of NSAIDs may have the potential to worsen HDP (due to the side effects of hypertension experienced by some users) and should therefore be used judiciously. While acetaminophen is thought to pose less risk in terms of elevation of blood pressure and provides reasonable pain relief for perineal pain, available research provides only limited information about side effects.

RECOMMENDATIONS

13. For clients with HDP whose blood pressure remains elevated upon discharge from hospital, midwives should ensure that a plan is in place with the consulting physician for follow-up consultation in the postpartum period if the client's blood pressure remains elevated and/or increases. (III-B)
14. Monitor blood pressure at all regularly scheduled postpartum visits for the first 2 weeks postpartum or until blood pressure has returned to normal for 2 consecutive visits for clients who have experienced HDP. (IIIB)
15. Following the birth, inform clients with HDP that their elevated blood pressure may take some time to resolve and that in some cases, gestational hypertension may worsen during the postpartum period (though this is relatively uncommon). Advise clients to page their midwife if signs and symptoms of preeclampsia develop in the postpartum period. (IIIA)
16. For clients with HDP, limit use of nonsteroidal anti-inflammatory drugs (ibuprofen, naproxen, diclofenac) for management of postpartum pain. Acetaminophen is an effective alternative, though available research provides only limited information about side effects. (IIIL)
17. Women who have had HDP should be advised that they may be at increased risk of developing hypertension or cardiovascular disease later in life. (III-B)
18. Midwives should discuss the positive benefits of a heart healthy diet and lifestyle with women who have had HDP, and how these factors may mitigate development of hypertension-related disease in later life. (IB)
19. Upon discharge from midwifery care, ensure information about a client's HDP is communicated to the primary care provider/family physician who will be providing ongoing care to the client, if applicable. (IIIB)

CONCLUSION

HDP includes a range of conditions of varying etiology, severity and symptoms. While these conditions rarely result in long-term harm for mother or baby, HDP is a major contributor to morbidity and mortality. The midwife plays a key role in monitoring for elevated blood pressure and other signs and symptoms of HDP throughout the pregnancy, intrapartum and postpartum periods. Furthermore, midwives may continue to provide monitoring and/or support to women whose care is managed in consultation with a physician or is transferred to a consultant, and to advocate on their behalf.

Despite extensive research, the onset of hypertension during pregnancy has proven difficult to predict, and for many of the clinical manifestations of HDP, optimal evidence-based strategies for detection, surveillance and management have yet to be determined. Efforts to improve understanding of HDP are crucial.

COMPLETE RECOMMENDATIONS

1. Presence or absence of known risk factors for preeclampsia should be determined and communicated to clients early in care. Consultations should be arranged as indicated by the CMO's IMDCTC. (IIIA/B)

2. In the absence of consensus and clear evidence about what criteria should be considered in determining a woman's level of preeclampsia risk, midwives are encouraged to consider the client's clinical picture and consensus-based criteria in discussions related to client risk status and whether or not to undertake any potential preventive measures. (IIIB)

3. If consistent with community standards, offer low-dose aspirin (81 mg/day) to women at increased risk of developing preeclampsia, beginning once the client's increased risk has been identified (ideally before 16 weeks' GA), and continuing until delivery. (IA)

4. Inform women whose dietary calcium intake is below recommend levels (< 1000 mg/day) and women who are at increased risk of developing hypertension that calcium supplementation appears to reduce the risk of preeclampsia. Recommend increased calcium intake (1000-2500 mg/day) through calcium supplementation or by consuming additional servings of foods high in calcium (equivalent to 1000-2500 mg/day). (IA/B)

5. Discuss signs and symptoms of preeclampsia during the prenatal period (see "Symptoms of Preeclampsia") and ensure that clients are aware of how to contact their midwife in the event these symptoms arise. (IIIA)

Recommended midwifery actions when elevated blood pressure is detected in the absence of proteinuria:

6. a) For non-severe hypertension (dBP < 110 mmHg), at least two serial BP measurements using the same arm should be recorded before a diagnosis of hypertension is made. (II-2B)
   b) If dBP is ≥ 90 mmHg and < 110 mmHg and dipstick urine testing is negative for proteinuria, blood pressure should be reassessed by repeat measurement. Midwives will use their judgment to determine an appropriate interval between measurements, based on the client's gestational age, risk factors and presence of other signs and/or symptoms of preeclampsia.
   c) Conducting the second reading in the home environment is recommended when possible to rule out white coat hypertension. (II-2B)
   d) If an automated BP measurement device has been used for the first measurement, perform the second reading using a mercury sphygmomanometer or an aneroid device. (II-2B)
   e) Urinary protein should also be reassessed by dipstick at the time of the second BP measurement. (IIIB)
   f) Two successive readings of a dBP of ≥ 90 mmHg require a medical consultation. (IIIA)

7. If sBP is ≥ 140 mmHg and < 160 mmHg and dBP < 90 mmHg, and dipstick urine testing is negative for proteinuria, assess whether the client has risk factors for transiently elevated sBP (e.g. stress, caffeine, recent exercise) and determine whether or not to reassess the client's BP within a shorter time interval based on the client's clinical picture, while advising the client to contact her midwife if any other signs and symptoms of preeclampsia develop in the meantime. As elevated sBP may be a precursor to the subsequent development of diastolic hypertension, a higher index of suspicion may be warranted for these clients. (IIIB)

8. For severe hypertension (dBP ≥ 110 mmHg, sBP ≥ 160 mmHg), with or without proteinuria, further investigation and/or prompt assessment in a hospital setting and consultation with an obstetrician is warranted (Category 3 IMDCTC). (IIIA)

Recommended midwifery actions when blood pressure is elevated and in the presence of proteinuria:

RECOMMENDATIONS, cont...

9. a) If dBP is ≥ 90 mmHg and < 110 mmHg and proteinuria (equivalent to ≥ 0.3 g/L or more or ≥ +1 on urine dipstick) is present, midwives should use their clinical judgment to determine whether or not a reassessment should occur at home or in hospital the same day to confirm hypertension and presence of proteinuria. (IIIB)
   b) If hypertension and proteinuria are confirmed, further investigation and/or medical consultation and transfer of care is warranted. (IIIA)

Recommended midwifery actions when urinary protein is elevated:

10. a) For urine dipstick values equivalent to ≥ 0.3 g/L (≥ +1 on urine dipstick) in addition to other signs or symptoms of preeclampsia, further investigation and/or a prompt medical consult should be arranged. (IIIA)
    b) If a urine dipstick value equivalent to ≥ 0.3 g/L (≥ +1 on urine dipstick) is noted in the absence of elevated blood pressure or other signs and symptoms of preeclampsia, repeat the dipstick urinalysis. Midwives will use their judgment to determine an appropriate interval between measurements, based on the client's gestational age and risk factors. Midwives may suggest that clients use an obstetric towelette before producing the second sample to reduce the likelihood of a false-positive result. If urine dipstick reading remains equivalent to ≥ 0.3 g/L, further investigation and/or a medical consult is indicated. (IIIC)

11. Active management of the third stage of labour with oxytocin is recommended and should be offered to women with HDP. (IA)

12. Ergonovine maleate should be avoided in the prevention and treatment of PPH in women with HDP if other suitable uterotonic drugs are available. (II-3D)

13. For clients with HDP whose blood pressure remains elevated upon discharge from hospital, midwives should ensure that a plan is in place with the consulting physician for follow-up consultation in the postpartum period if the client's blood pressure remains elevated and/or increases. (III-B)

14. Monitor blood pressure at all regularly scheduled postpartum visits for the first 2 weeks postpartum or until blood pressure has returned to normal for 2 consecutive visits for clients who have experienced HDP. (IIIB)

15. Following the birth, inform clients with HDP that their elevated blood pressure may take some time to resolve and that in some cases, gestational hypertension may worsen during the postpartum period (though this is relatively uncommon). Advise clients to page their midwife if signs and symptoms of preeclampsia develop in the postpartum period. (IIIA)

16. For clients with HDP, limit use of nonsteroidal anti-inflammatory drugs (ibuprofen, naproxen, diclofenac) for management of postpartum pain. Acetaminophen is an effective alternative, though available research provides only limited information about side effects. (IIIL)

17. Women who have had HDP should be advised that they may be at increased risk of developing hypertension or cardiovascular disease later in life. (III-B)

18. Midwives should discuss the positive benefits of a heart healthy diet and lifestyle with women who have had HDP, and how these factors may mitigate development of hypertension-related disease in later life. (IB)

19. Upon discharge from midwifery care, ensure information about a client's HDP is communicated to the primary care provider/family physician who will be providing ongoing care to the client, if applicable. (IIIB)

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