



Pre-eclampsia

A risk factor for pre-term birth, low birth weight and neonatal mortality

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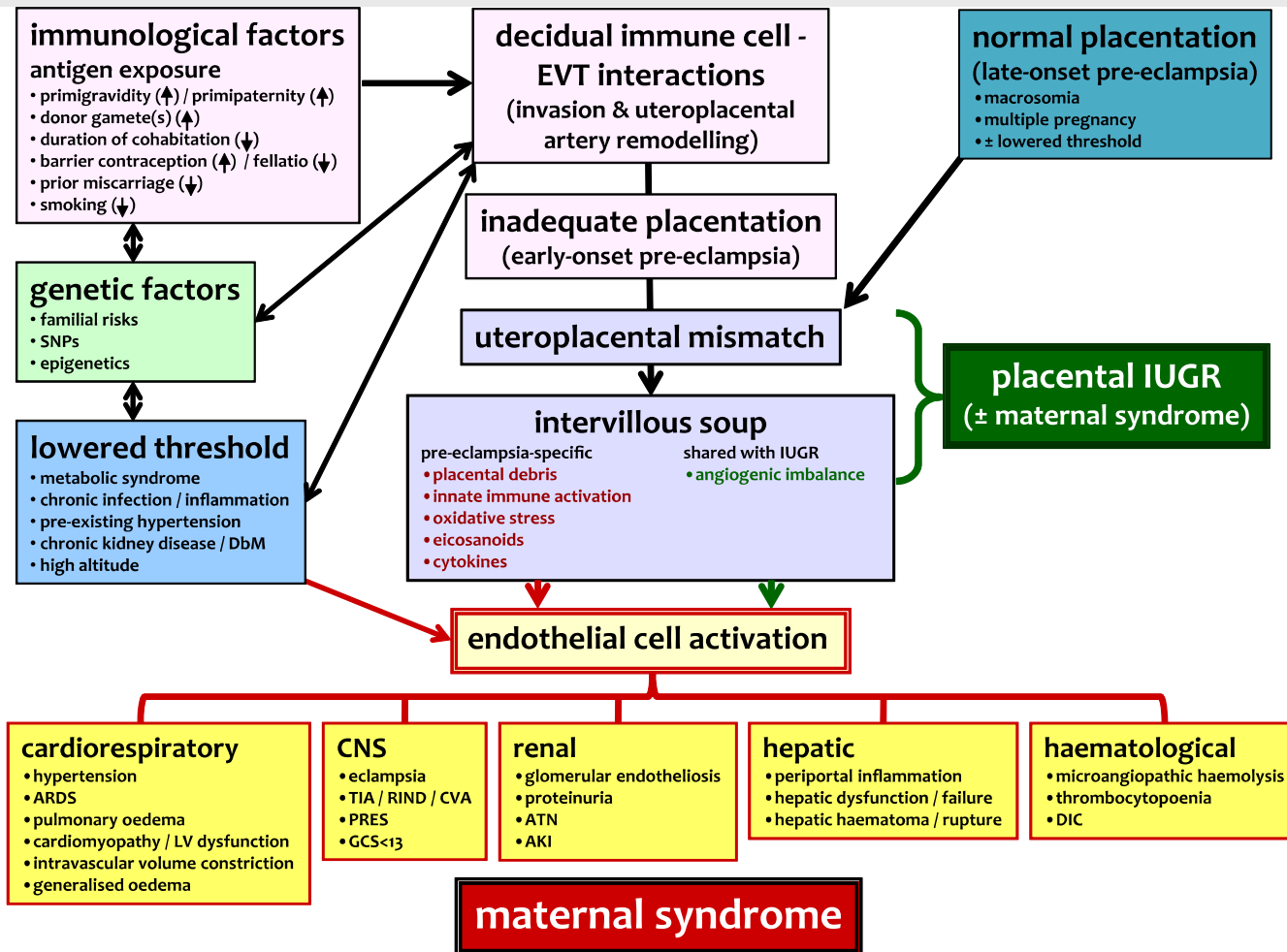


Objectives

1. Outline the pathophysiology of pre-eclampsia and its natural history
2. Describe the epidemiology of perinatal morbidity and mortality related to pre-eclampsia
3. Highlight the gaps and identify potential areas for research and action



Pathophysiology of Pre-eclampsia





Pre-eclampsia and Feto-placental Implications

Adverse conditions	Severe complications
<ul style="list-style-type: none">○ Non-reassuring fetal heart rate○ IUGR○ Oligohydramnios○ Absent or reversed end-diastolic flow by Doppler velocimetry	<ul style="list-style-type: none">○ Abruptio with evidence of maternal or fetal compromise○ Reverse ductus venosus A wave○ Stillbirth



Natural History of Pre-eclampsia

- 2 RCTs (133 women) show that expectant care of severe pre-eclampsia was associated with a mean pregnancy prolongation of 2.0 weeks [1.4, 2.6] ¹
- A 2009 systematic review found that expectant care of severe preeclampsia <34 weeks (39 cohorts, 4,650 women) was associated with pregnancy prolongation of 7-14 days²

¹Obstet Gynecol 1990;76:1070-5; AJOG 1994;171:818-822

²Hypertens Pregnancy 2009;28(312-47).



Diagnosis, evaluation, and management of the hypertensive disorders of pregnancy




CrossMark



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On behalf of the Canadian Hypertensive Disorders of Pregnancy (HDP) Working Group¹

Severe complications (that warrant delivery)



- Eclampsia
- PRES
- Cortical blindness or retinal detachment
- Glasgow coma scale < 13
- Stroke, TIA, or RIND
- Uncontrolled severe hypertension (over a period of 12hr despite use of three antihypertensive agents),
- Oxygen saturation < 90%, need for \geq 50% oxygen for > 1hr, intubation (other than for Caesarean section), pulmonary oedema
- Positive inotropic support
- Myocardial ischaemia or infarction
- Platelet count < $50 \times 10^9/L$
- Transfusion of any blood product

- Acute kidney injury (creatinine > 150 μM with no prior renal disease)
- New indication for dialysis
- Hepatic dysfunction (INR > 2 in absence of DIC or warfarin)
- Hepatic haematoma or rupture

- Abruptio with evidence of maternal or fetal compromise
- Reverse ductus venosus A wave [85,86]
- Stillbirth



Pre-eclampsia and Perinatal Outcomes

**Spontaneous
Pre-term Birth**

**Provider
Initiated
Pre-term
Birth**

IUGR

**Low birth
weight**

**Neonatal
death**

Stillbirth



Provider Initiated Pre-term Birth

Hypertension is the leading cause of provider-initiated preterm delivery^{1,2}

- EMIP³: Hypertensive disorders (pre-eclampsia 58.2%, chronic hypertension 15.3%, gestational hypertension 12.9%, and HELLP syndrome 9.4%) were the most common indications of provider initiated pre term delivery
- WHO Multi-Country Survey²: pre-eclampsia (18.2% vs 2.6%, $p < 0.001$) was higher in women with provider initiated pre-term birth²

¹ BJOG 121 Suppl: 101-9

² BMC Pregnancy and Childbirth 2014, 14:56

³ PLoS ONE 11(2): e0148244



Geography of Pre-eclampsia related Pre-term Birth

- Pre-eclampsia rates vary nationally, regionally and globally
- Hypertensive disorders were associated with both spontaneous and indicated preterm birth in all Human Development Index groups
- The risk of preterm delivery caused by these complications did not decrease despite higher levels of country development

Maternal condition	All countries (%)***	Very high HDI (%)****	High HDI (%)****	Medium HDI (%)****	Low HDI (%)****
(A) Prevalence of selected maternal medical conditions					
Anaemia	4077 (1.4)	181 (1.0)	164 (1.7)	208 (1.4)	151 (1.2)
Infection					
Pyelonephritis	453 (0.2)	18 (0.1)	96 (0.1)	235 (0.2)	104 (0.1)
Puerperal endometritis	270 (0.1)	93 (0.6)	67 (0.1)	58 (0.1)	52 (0.0)
Systemic infection	966 (0.3)	137 (0.8)	249 (0.4)	355 (0.4)	225 (0.2)
HIV/AIDS	1109 (0.4)	27 (0.2)	86 (0.1)	113 (0.1)	883 (0.8)
Malaria/dengue	312 (0.1)	2 (0.0)	13 (0.0)	52 (0.1)	245 (0.2)
Hypertensive disorders					
Chronic hypertension	1148 (0.4)	83 (0.5)	346 (0.5)	446 (0.4)	273 (0.2)
Pre-eclampsia/eclampsia	7066 (2.4)	445 (2.7)	1908 (2.9)	2811 (2.9)	1902 (6)
(B) Adjusted odds ratios and 95% confidence intervals for estimates of effect of maternal medical conditions on preterm delivery					
Anaemia	2.0 (1.8; 2.2)**	2.0 (1.3; 3.0)*	1.8 (1.3; 2.5)*	2.0 (1.7; 2.3)**	2.3 (2.0; 2.7)**
Infection					
Pyelonephritis	1.5 (1.1; 2.0)*	0.6 (0.1; 5.4)	6.4 (3.5; 12)**	1.3 (0.8; 2.1)	1.1 (0.7; 1.9)
Puerperal endometritis	1.8 (1.2; 2.7)	0.4 (0.1; 1.3)	3.7 (1.9; 7.1)**	1.5 (0.6; 3.8)	2.7 (1.3; 5.8)*
Systemic infection	2.8 (2.3; 3.4)**	1.6 (0.8; 3.1)	5.8 (3.9; 8.6)**	2.4 (1.8; 3.2)**	2.7 (1.9; 4.0)**
HIV/AIDS	1.2 (1.0; 1.5)	5.5 (2.0; 15)*	1.4 (0.6; 3.5)	1.0 (0.5; 1.9)	1.2 (0.9; 1.6)
Malaria/dengue	4.4 (3.2; 6.13)**	NE****	3.2 (0.5; 19)	2.5 (1.3; 4.8)**	5.4 (3.6; 8.0)**
Hypertensive disorders					
Chronic hypertension	2.3 (1.9; 2.7)**	3.0 (1.5; 6.0)*	3.3 (2.5; 4.3)**	2.3 (1.8; 2.9)**	1.1 (0.8; 1.7)
Pre-eclampsia/eclampsia	5.0 (4.7; 5.4)**	5.0 (3.8; 6.6)**	6.1 (5.4; 6.9)**	3.7 (3.3; 4.1)**	6.7 (5.9; 7.5)**



Pre-eclampsia and Perinatal Death

- 9-20% of perinatal deaths are reported to be a direct result of the hypertensive disorders of pregnancy¹
- Adverse perinatal outcomes, including stillbirth, are modified by gestational age with the risk of perinatal death being highest at earlier gestational ages^{1,2,3}
- Risks of stillbirth and early neonatal death lower in spontaneous preterm deliveries compared with provider-initiated deliveries⁴

¹FIGO Textbook of the Hypertensive Disorders of Pregnancy

²BMC Pregnancy and Childbirth 2014, 14:56

³PLoS ONE 11(2): e0148244

⁴BJOG 2014 Mar;121 Suppl 1:101-9



Chronic Hypertension and Adverse Perinatal Outcomes

Outcome	No of studies	Estimated incidence (%) (95% CI)	Prediction intervals (95%)	Heterogeneity τ^2
Superimposed pre-eclampsia	38	25.9 (21.0 to 31.5)	5.5 to 67.2	0.766
Caesarean section	27	41.4 (35.5 to 47.7)	15.5 to 73.2	0.413
Pre-term delivery (<37 weeks)	30	28.1 (22.6 to 34.4)	6.8 to 67.6	0.286
Birth weight <2500 g	14	16.9 (13.1 to 21.5)	5.7 to 40.6	0.286
Neonatal intensive care	16	20.5 (15.7 to 26.4)	5.9 to 51.3	0.403
Perinatal death	27	4.0 (2.9 to 5.4)	0.9 to 16.4	0.544

Bramham et al. BMJ 2014;348:g2301



Summary

- Pre-eclampsia is associated a number of adverse perinatal outcomes
- Pre-eclampsia is associated with both spontaneous and provider initiated pre-term birth
- The spectrum of the hypertensive disorders of pregnancy, particularly chronic hypertension, should be considered for pre-term birth, low birth weight and neonatal mortality



Discussion: Gaps

- Regional variations: pre-eclampsia prevalence and rates of provider initiated pre-term delivery
- Provider initiated pre-term delivery: exploration of reasons for delivery
- Severe hypertension: optimal and timely management
- Chronic hypertension: pre conception counseling
- Pre-eclampsia risk modification and surveillance