Vertical Integration
Case study “ Asking for Help”

Dr Renée Pope

Learning outcomes

1. Define chronic hypertension, gestational hypertension, preeclampsia
2. Outline the management of HELLP and Preeclampsia
3. Review risk of future episodes of preeclampsia in future pregnancys

One Thursday morning…

- A 29 y.o Female G1P0 36 +2 sent in for review by the midwife with *48 hours of severe* banding bilateral *upper abdomen/ thoracic pain.* Accompanied by her husband.

- Mid wife was wanting her to attend for GP review as she was worried she could have pneumonia

Continued…

- Thoracic pain – described as banding around from the back and wrapping around her chest anteriorly
- Gradually worsening over the past 2 days
- Associated pleuritic type pain on deep breathing
- Reproducible when moving
- Pain so severe waking her from sleep – found worse in the morning
- Having Panadol 1g q4hrly to maximum dosage for the past 2 days
- Watching the clock for the next dose - “ I’m in severe pain – can you help?”

Continued…

No recent coryzal/ URTI symptoms

No changes to vision. No headache

No epigastric pain

No changes to bowel habit

No urinary symptoms

No sudden onset peripheral oedema

No previous back injury

Examination

- SpO2 98, RR 16, HR 68, BP 145/80
- Appeared well groomed, teary, preferring to stand due to pain
- Talking in full sentences
- No increased WOB/ Accessory muscle use
- Chest was clear in axillar and to bases bilaterally
- HSDNM
- No skin changes
- No point tenderness over thoracic spine
- Some tenderness to palpation over RUQ/ LUQ
- Reported normal foetal movements

Differentials

- MSK – Lat dorsi/ Serratus anterior pain
  - Positional
  - Tender on palpation
- Resp – Pneumonia
  - No proceeding symptoms
- Resp – PE
  - D-Dimer elevated – CT in pregnancy? V/Q scan?
- Cardiac – dissection
- Gastric – Liver
  - Choledocholithiasis
- Hypertension
- Neuro – unlikely
- Infective – Pyelonephritis/ UTI

Hypertension

Definition of hypertension in pregnancy

- Systolic blood pressure (SBP) of ≥140mmHg or a diastolic blood pressure (DBP) ≥90mmHg.
    - The blood pressure (BP) must be elevated on two occasions at least four hours apart
- Detecting a rise in BP from ‘booking’ or preconception BP >30/15mmHg useful in women who do not reach above definition
- Severe Hypertension(HTN): SBP ≥ 170mmHg and/or DBP ≥ 110mmHg
    - Commence treatment in severe HTN in pregnancy > 160/100 mmHg
- Urgent treatment >170/110 mmHg
    - cerebral perfusion pressure, susceptible to cerebral hemorrhage, posterior reversible encephalopathy syndrome and Hypertensive encephalopathy

Chronic Hypertension	Gestational Hypertension	Preeclampsia superimposed on chronic hypertension
<u>Essential Hypertension</u>: SBP of ≥140mmHg or DBP ≥90mmHg. Before pregnancy or before 20 weeks without a known cause **<u>Secondary causes include:</u>** **Renal causes;** (glomerulonephritis, diabetic nephropathy, reflux nephropathy, polycystic kidney disease) **Vascular causes;** (coarctation of the aorta, renal artery stenosis) **Endocrine causes;** phaeochromocytoma, primary aldosteronism, Cushing's syndrome, hypothyroidism, hyperthyroidism, polycystic ovary syndrome, hyperparathyroidism	New onset HTN ≥20 weeks No maternal or foetal features of preeclampsia • Up to 25% of women will develop Return of BP to normal within 12 weeks post-partum. If BP increased >12 weeks post-partum, classify as chronic HTN	Defined as chronic hypertension with the additional features of pre-eclampsia Pre-existing HTN strong risk factor for Preeclampsia Superimposed Preeclampsia >20 weeks in a woman with chronic HTN

Ongoing investigation of women with hypertension in pregnancy

	Modality	**Frequency**
Chronic hypertension	Assess for proteinuria* Preeclampsia bloods**	Each visit If sudden increase in BP or new proteinuria
Gestational hypertension	Assess for proteinuria Preeclampsia bloods	1-2x/week Weekly
Preeclampsia	Assess for proteinuria Preeclampsia bloods	At time of diagnosis: if non-proteinuric repeat daily* Twice weekly or more frequent if unstable

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What would you do next?

- Bedside Urinalysis
  - Nitrates –ve
  - Leukocytes –ve
  - Glucose –ve
  - Protein +

Sent with pathology form
EUC/LFT; FBC; ESR; CRP; Iron Studies.

Urine protein / albumin.
Marked as ** Urgent** - call with results

Instructed her to attend local pharmacy in 4 hours to retake blood pressure – see if resolving

Continued on with day

What I did…

- Pain management
  - Discussed lifestyle recommendations – hot or cold
  - Continue Panadol
  - Opioids?
  - Physiotherapy

- Social
  - Well supported husband
  - Linked into to midwifery program – low risk

Kennedy, D, Analgesics and pain relief in pregnancy and breastfeeding, (Aust Prescr 2011;34:8–10)
https://www.nps.org.au/assets/f4cd8a064d47b62a0e01df33044e139fddfcb7c79fd0c38a7065fad62081b237334047fed3a63e4463e31f34.pdf

LATER that morning

Follow up to Pathology company

- Liver biochemistry machine was broken so had sent to Sydney for overnight results

- FBC and coagulation studies were back…

Haematology

Haemoglobin	110	g/L	(100 - 160) #
Red cell count	3.6	x10^12/L	(3.4 - 5.8) #
Haematocrit	0.31		(0.30 - 0.48) #
MCV	86	fL	(80 - 100)
MCH	30.9	pg	(27.0 - 32.0) #
MCHC	358	g/L	(310 - 360)
RDW	12.2		(10.0 - 15.0)
White cell count	12.4	x10^9/L	(4.0 - 16.0) #
Neutrophils	9.64	x10^9/L	(2.0 - 13.0) #
Lymphocytes	1.51	x10^9/L	(1.0 - 4.0)
Monocytes	1.12	x10^9/L	(0.0 - 1.2) #
Eosinophils	0.05	x10^9/L	(0.0 - 0.5)
Basophils	0.03	x10^9/L	(0.0 - 0.3)
NRBC	<1.0	/100 WBC	(<1)
Platelets	L 59	x10^9/L	(150 - 450)

#Please note reference limits apply to Pregnancy at the specified date of collection.

Red Cell Morphology: Normal

Moderate thrombocytopenia

Occasional large platelets

Unauthorised Report - Completed Report to Follow

30/11/2023 4:05 pm

Coagulation Studies

PT	13	s	(9 - 13)
INR	1.1		(0.9 - 1.2)
APTT	30	s	(20 - 32)
Thrombin Time	16	s	(15 - 22)
Fibrinogen	H 4.9	g/L	(1.5 - 4.2)

Comment: Increased fibrinogen - probable inflammatory response.

Preeclampsia

Pathophysiology

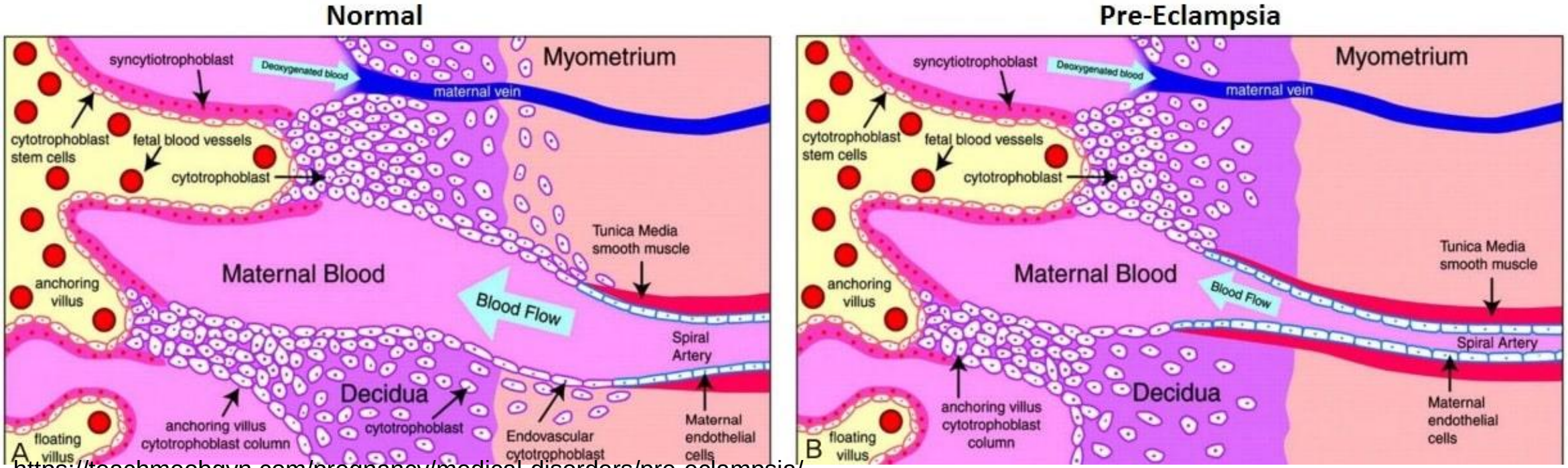
Is a disease of the placenta

Current theories suggest related to poor placental perfusion.

Associated with failure of normal invasion of trophoblast cells leading to maladaptation of uterine spiral arterioles.

The poor vascular invasion of the results in placental dysfunction

Increase in blood pressure, combined with hypoxia and oxidative stress from inadequate uteroplacental perfusion, leads to a systemic inflammatory response and endothelial cell dysfunction (resulting in leaky blood vessels).



https://teachmeobgyn.com/pregnancy/medical-disorders/pre-eclampsia/

Preeclampsia Classification

- Internationally – ISSHP no longer requires proteinuria for diagnosis of preeclampsia. British NICE guideline has this requirement.
- Multi system disorder unique to human pregnancy characterised by hypertension and involvement of one or more other organ systems and / or fetus.
  - Hypertension - common but not always first manifestation
  - Proteinuria – common but not mandatory
- > 20 weeks gestation and is accompanied with one or more of the following signs of organ involvement
  - Renal involvement
  - Haematological involvement
  - Liver involvement
  - Neurological involvement
  - Pulmonary oedema
  - Fetal growth restriction (FGR)

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Quiz

- Which of the following is classified as a high-risk factor for developing pre-eclampsia during pregnancy?
- Family history of pre-eclampsia
- Chronic hypertension
- Multiple pregnancy
- Maternal age ≥ 40 years

https://teachmeobgyn.com/pregnancy/medical-disorders/pre-eclampsia/

Risk Factors

Risk factors associated with preeclampsia

Risk Factor	Unadjusted Relative Risk [95% CI]
Nulliparity	2.9 [1.3-6.6]
Multiple pregnancy	2.9 [1.3-6.6]
Previous history of preeclampsia	7.2 [5.9-8.8]
Family history of preeclampsia	2.9 [1.7-4.9]
Overweight BMI 25-29.9*	1.7 [1.2-2.4]
Obese BMI >30*	2.7 [1.7-4.4]
Age ≥ 40	2.0 [1.3-2.9]
Systolic BP>130mmHg before 20 weeks	2.4 [1.8-3.2]
Diastolic BP >80mmHg before 20 weeks	1.4 [1.0-1.9]
Antiphospholipid syndrome	9.7 [4.3-21.8]
Pre-existing diabetes	3.6 [2.5-5]
Other risk factors	Underlying renal disease Chronic autoimmune disease Interpregnancy interval >10 years

Protective for preeclampsia –

- Miscarriage with the same partner in nulliparous women
- High fruit intake
- Smoking (not in women with chronic hypertension)
- Taking greater than 12 months to conceive

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Clinical Features

Symptoms

- Headache (?Frontal)
- Visual disturbance
- Nausea and vomiting
- Epigastric/RUQ pain

Mild Pre-eclampsia is frequently asymptomatic and without physical signs

Signs

- Hyperreflexia
- Clonus
- Epigastric/RUQ tenderness
- Severe peripheral oedema

Complications

- HELLP syndrome (syndrome of Haemolysis, Elevated Liver enzymes & Low Platelets) –really a variant of severe PET rather than complication
- Eclampsia
- Haemorrhagic stroke
- Placental abruption
- Stillbirth
- DVT/PE
- AKI

Investigations

- Urine dipstick
  - Proteinuria (+1 protein)→ Spot Urine PCR
  - 24-hour urine collection for protein:creatinine ratio
    - Urinary excretion ≥0.3 g protein in 24 hrs; or urine protein:creatinine ratio ≥30 mg/mmol; or normal

- Pre-eclampsia bloods
  - FBC, EUCs, LFTs, urate (may in elevate), coagulation screen
    - Thrombocytopenia, raised serum creatinine, elevated transaminases, elevated uric acid

- Ultrasound
  - Foetal growth, FI (amniotic fluid index), uterine artery (UA) doppler flow

Case study

- Attended Birth unit
- Repeat Pathology

HELLP Syndrome

HELLP Syndrome

- First named in 1982 by Dr. Louis Weinstein
- **Ha**emolysis, **E**levated **L**iver enzymes, **L**ow **P**latelets Syndrome
- Considered a variant or complication of Pre-eclampsia
- Liver endothelial dysfunction that results in consumptive coagulopathy
- Microangiopathic haemolytic anaemia

https://www.aafp.org/pubs/afp/issues/2018/0915/p354.html#afp20180915p354-t1

HELLP Syndrome

- Prevalence of 0.5-0.9% pregnancy's
- 70% of cases occur in 3rd trimester
- 30% of cases, it can present post partum, typically within the first 48 hours of delivery
- Mortality rate reported between0 – 24%, perinatal death up 37%

Risk Factors for HELLP

- Preeclampsia
- Eclampsia
- Family History of preeclampsia or HELLP syndrome
- Autoimmune conditions (? SLE)
- Clotting disorders (Factor V – evidence lacking)

QUIZ

- Which of the following anti-hypertensive medications is first line in the management of pre-eclampsia (assuming no other maternal comorbidities)?
- Nifedipine
- Methyldopa
- Labetalol
- Ramipril

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Management - Gestational hypertension

Lifestyle modification

- If lifestyle medications fail to control BP; Antihypertensive medication (methyldopa or labetolol)
- If severe HTN - IV hydralzine or labetolol

Induction of labour/delivery if indicated

Table 5. Guidelines for selecting antihypertensive drug treatment in pregnancy

Drug	Dose	Action	Contraindications	Practise Points
Methyl dopa	250-750mg tds	Central	Depression	Slow onset of action over 24 hours, dry mouth, sedation, depression, blurred vision
Clonidine	75-300µg tds			Withdrawal effects: rebound hypertension
Labetalol	100-400mg q8h	β Blocker with mild alpha vasodilator effect	Asthma, chronic airways limitation	Bradycardia, bronchospasm, headache, nausea, scalp tingling (labetalol only) whic usually resolves within 24 hours
Oxprenolol	20-160 mg q8h	β Blocker with intrinsic sympathomimetic activity		
Nifedipine	20mg -60 mg slow release bd	Ca channel antagonist	Aortic stenosis	Severe headache in first 24 hours Flushing, tachycardia, peripheral oedema, constipation
Prazosin	0.5-5 mg q8h	α blocker		Orthostatic hypotension especially after first dose
Hydralazine	25-50 mg q8h	Vasodilator		Flushing, headache, nausea, lupus-like syndrome

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Management – Pre-Eclampsia

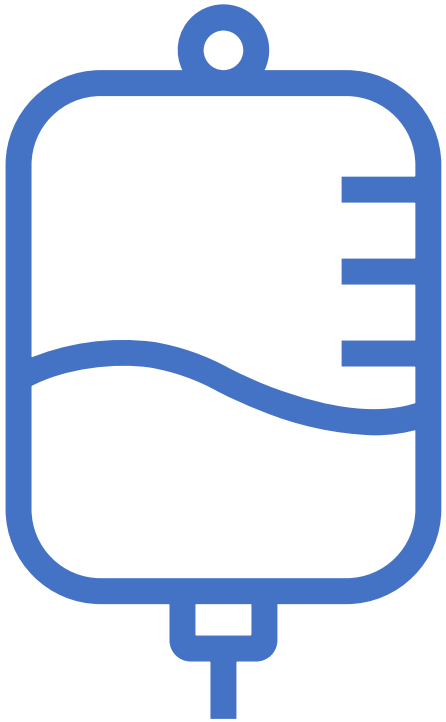

Table 3. Timing of delivery and gestation of presentation of preeclampsia

Gestation at onset	Previable <23^{6} weeks	24-31^{6} weeks	32-36^{6}	37+0 onwards
Delivery plan	Consult with Tertiary institution: likely to need termination of pregnancy or extreme preterm delivery. High risk patient	Consult and transfer to Tertiary institution: likely to need preterm delivery. Aim to prolong pregnancy where possible	Aim to prolong pregnancy where possible, deliver in institution with appropriate Paediatric care	Plan delivery on best day in best way

- Delivery is definitive management
- If < 32 weeks – tertiary institute involvement – NICU requirements
- Immediate Management – delivery planned withing 48 hours after BP stabilisation, Corticosteroid administered for foetal maturation +/- Magnesium sulphate for neonatal neuroprotection
- Expectant Management – Prolongation of pregnancy beyond 48 hours with maternal and foetal monitoring
  - **Prolongation is for foetal benefit
  - If <24 weeks : increased maternal mortality of 65 – 71% and Perinatal mortality > 80%
  - 34 – 36 weeks – at increased risk of LSCS, RDS, NICU admissions
  - 40% of women are eligible for expectant care
    - 25 – 41% of women will develop severe morbidity –HELLP, Abruption, Pulomnary oedema, eclampsia

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Table 4. Indications for delivery in women with preeclampsia or gestational hypertension

Maternal	Fetal
Gestational age ≥ 37 weeks	Placental abruption
Inability to control hypertension	Severe FGR
Deteriorating platelet count	Non-reassuring fetal status
Intravascular haemolysis	
Deteriorating liver function	
Deteriorating renal function	
Persistent neurological symptoms	
Persistent epigastric pain, nausea or vomiting with abnormal LFTs	
Pulmonary edema	

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Other considerations

- Thromboprophylaxis
- Fluid management
- Haematological manifestations
- Hepatic manifestations

Management – Case Study

- Emergency Caesarean at 2300
- Discussion with haematology – 1-unit pooled platelet prior to operation
- General anaesthetic due to plts 59 pre op
- Cephalic presentation. Live male infant. Clear liquor
- Normal ovaries./ tubes
- EBL 400ml
- Returned to ICU post op for blood pressure monitoring

Management - Case Study

- BP stable – discharged to ward
- Platelets continued to down trend
- Suspected TTP? Haematology involvement – received right sided IJ vascath with platelets x1
- Underwent Plasma exchange (PLEX)
- Adams T 13 - negative
- No ongoing Clinical signs for TTP
- No for further PLEX
- Discharged from ICU again
- Analgesia – Panadol and oxycodone (not for ibuprofen → kidneys!)
- Discharged home

Management – Post partum

- **First 6 weeks**

1. Pre-existing HTN – often unstable immediately after delivery, may require medication adjustment. Avoid NSAIDs post partum – AKI/ CKD or in setting of thrombocytopenia.
2. Sustained hypertension post partum (> 6 weeks)more common with long duration of antihypertensive treatment in pregnancy, higher BMI, preterm preeclampasia.
3. Normally stabilises in first 2 months following pregnancy and treatment
4. ACE-I , enalapril, captopril and quinapril are compatibile with breast feeding,

- **After 6 weeks**

1. ? need for further investigations. Renal disease
2. Ensure normalisation and albuminuria post-partum
3. Obese, CVD risk , secondary htn and end organ disease

9 days later…

Presents to her Regular GP for review at 1.5 weeks post-partum with emergency LSCS at 36 weeks for HELLP syndrome.

1. Blood Pressure
    - on Labetolol for BP 200mg bd with a view to wean over next few weeks
    - Follow up of blood pressure with midwife visit –BP110/70
2. Mental Health
    - Post birth counselling/ trauma debriefing – in shock and comprehending what happened

3. Pathology – Reviewed weekly

Male Bub –

- Birth weight 2980g
- APGARs 6, 8, 9
- didn't require SCN
- Exclusively breast feeding now.
- Vitamin K given
- Declined Hep B but will have at 6 week check

Examination: BP (sitting): 110/80
bruising around scar (from low plts) but healing well, Abdomen Soft

At next few weekly checks

- Labetolol continuing to wean by 50mg
- Keflex for wound ooze

6 week check

- Blood pressure stabilised (113/73, 117/71 , 127/77 (the highest it has been)
- Scar healing well, didn’t require antibiotics
- Breastfeeding ~3hrly
- PV bleeding resovled
- Contraception discussed - preference voiced for copper IUD/ non hormonal option
- EPND – score of 8, feels MH improving
- Continues to have good supports – husband 12 weeks off work – 6 weeks to go

Examination:

- **General:**

BP (sitting): 118/75

Abdomen soft, scar healing well. a few scabs (no sutures visible)

Followed up in Gynae clinic 8 weeks post

- Debrief on birth events
- Review of pathology – Hb 139, plts 401, LFTs and Renal functiosn normalised
- Plan for next pregnancy – 20% recurrence risk for pre-eclampsia
- Commence aspirin 150mg daily ~14 weeks gestation – will reduced her risk of pre-eclampsia by approx. 50%
- Contraception commenced
  - Discussed copper IUD vs Mirena
  - Follow up arranged to Mirena insertion
- Wound healing well

Recurrence and Future pregnancy

	Recurrence risk in subsequent pregnancies	
	Gestational hypertension	Preeclampsia
Previous gestational hypertension	16-47%	2-7%
Previous proteinuric preeclampsia	13-53%	16%
Severe preeclampsia <34 weeks <28 weeks		 25% 55%

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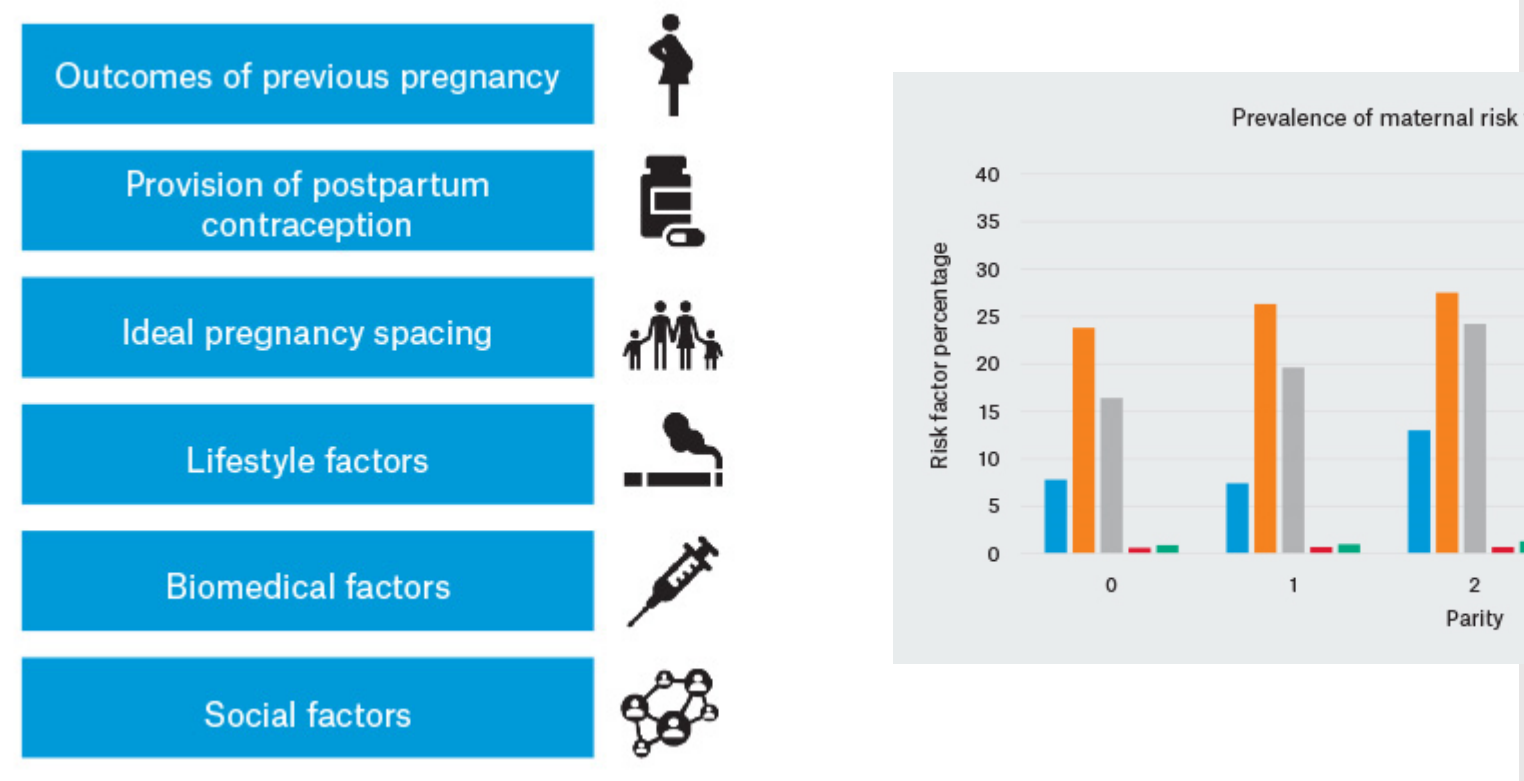
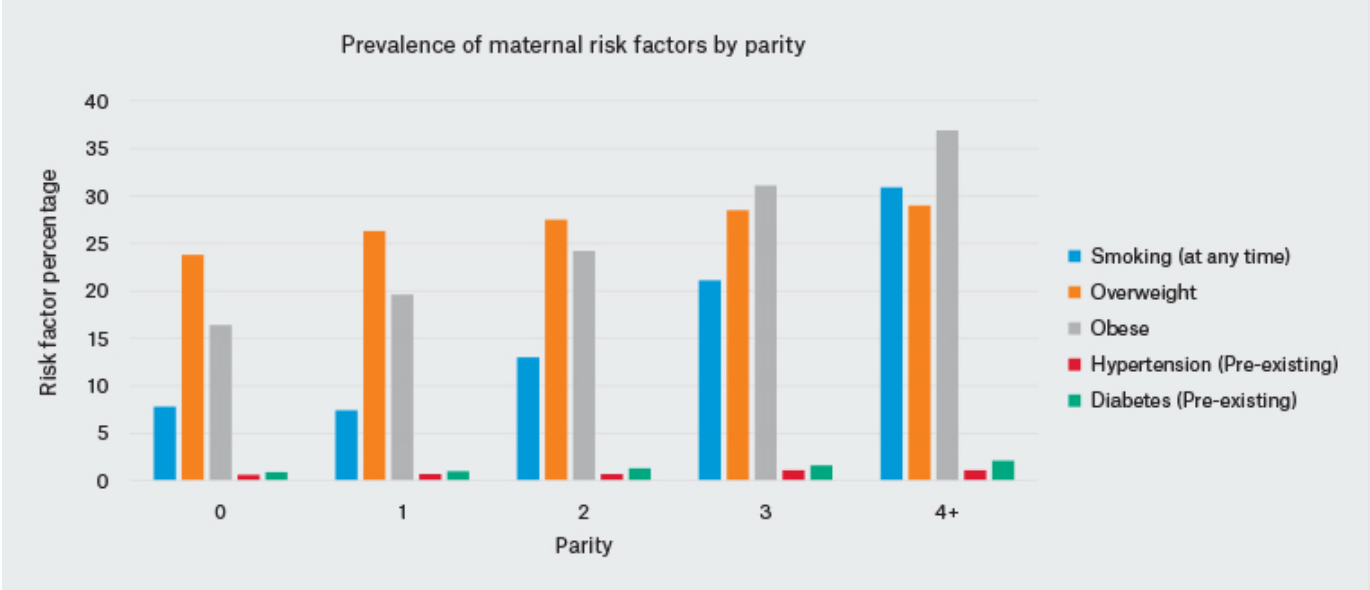
Inter-conception care





https://www1.racgp.org.au/ajgp/2020/june/interconception-care#:~:text=Optimising%20health%20before%20the%20next,prior%20to%20the%20next%20pregnancy.
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Box 1. Preconception care checklist[33]

Diet

- Discuss nutritional requirements including folic acid supplementation
- Provide advice about a healthy diet

Weight

- Measure body mass index and provide appropriate advice

Exercise

- Advise 150 minutes of exercise per week or 30 minutes on most days

Pregnancy history

- Screen for any modifiable risk factors

Genetic screening

- If indicated from personal/family history or ethnic background, discuss genetic carrier screening

Smoking/alcohol/illicit drugs

- Assess intake and provide appropriate advice

Psychosocial aspects

- Screen for domestic violence
- Screen for mental health conditions

Medical conditions

- Review current disease status and medications
- Referral/correspondence with specialist if required

Environmental

- Assess work, home and recreational environments

Contraception/family planning

- Offer appropriate contraception advice for those not desiring pregnancy

Breast examination

Dental health check

Screening for sexually transmissible infections and other infectious diseases

- Measles, mumps, rubella, varicella zoster, hepatitis B, syphilis
- Human immunodeficiency virus and hepatitis C with appropriate pre-test counselling
- Cervical screening

Table 8 Outcomes of pregnancy in women with chronic hypertension (58)

Outcome	All	No preeclampsia	With superimposed preeclampsia
Preeclampsia	22%*		
Preeclampsia <34/40	9.7%		
Preterm birth <37/40		15%	51%
Preterm birth <34/40		7%	23%
Caesarean section	50%	44%	70%
SGA	27%	21%	48%
BW <2.5kg	20%	13%	44%
Need for additional antihypertensive medication	Oral 24% Parental 4%		

LDA: low-dose aspirin;* On LDA: 28%; no LDA: 21% [NS] SGA: <10th centile using customised growth charts, BW = birth weight,