Clinical Guideline MANAGEMENT OF SICKLE CELL DISEASE IN PREGNANCY

SETTING	Trust wide
FOR STAFF	Midwifery and Medical staff
PATIENTS	Pregnant women with Sickle Cell Disease, their partners and neonates

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Pre-pregnancy Counselling

Women (of childbearing age) and men with haemoglobinopathies should be offered preconceptual counselling with their haematologist. Discussion should cover risks and implications of inheritance of their condition and review of medications. If there is a risk of a major haemoglobin disorder, couples should be counselled about their reproductive options including non-intervention, prenatal diagnosis or Pre-implantation Genetic Diagnosis (PGD). All women considering pregnancy should be referred for pre-pregnancy counselling by a maternal medicine consultant with expertise in managing SCD in pregnancy. This counselling should include the following discussion points:

Effect of pregnancy on sickle cell disease:

- Worsening of anaemia
- Increased rates of painful crises and chest syndromes
- Increased rate of infections especially urinary tract infections and postpartum uterine infections
- Increased maternal demands (i.e. if cardiomyopathy secondary to previous iron overload)

Effect of sickle cell disease on pregnancy:

- Increased miscarriage and stillbirth rates
- Increased risk of intra-uterine growth restriction
- Increased risk of premature labour and consequences of prematurity
- Increased risk of thromboembolic disease
- Increased risk of pre-eclampsia

Medications for sickle cell disease:

- Hydroxycarbamide (hydroxyurea) should be discontinued a minimum of 3 months prior to conception due to teratogenicity risk (unless a woman is at high risk of serious complications and blood transfusion is not feasible)
- Chelation therapy should usually be stopped prior to conception. If there is evidence of significant iron overload pre-conception, pregnancy should be delayed to allow for aggressive iron chelation prior to conception.
- A plan should be made for discontinuation/conversion of Angiotensin-converting enzyme inhibitors guided by strength of indication and likelihood of early pregnancy confirmation. Angiotensin receptor blockers should usually be stopped before conception, but alternative medications will need to be discussed in conjunction with a cardiologist.
- Analgesia and effects on fetus (NSAIDs and opioids) should be discussed. Ideally NSAIDS should be avoided before 14 weeks and after 32 weeks gestation.
- > Effects of any other medications should be discussed

Fetal implications of maternal sickle cell disease:

- Perinatal mortality is increased (4-6% in UK). This does not correlate with maternal anaemia and is not improved by transfusion therapy.
- Partner screening and genetic counselling Fetus has a 50% risk of major haemoglobin disorder if the partner carries a significant Hb disorder.

Optimisation of conditions to encourage a healthy pregnancy in sickle cell disease patients:

- Folic acid 5mg od (note higher dose due to risk of folate deficiency secondary to chronic haemolysis) should be commenced prior to conception and continued throughout pregnancy
- Vitamin D 10 micrograms daily, as per national recommendations for pregnancy
- Prophylactic penicillin (or suitable alternative if allergic to penicillin) for infections associated with hyposplenism
- Assessment of organ dysfunction due to iron overload by cardiac and liver T2* MRI (chelation may be advised prior to embarking on pregnancy)
- Endocrine function review: oral glucose tolerance test/HbA1c, fructosamine levels if diabetic on regular transfusions and thyroid function test
- Review of vaccination status (*H.influenza* type b, meningocococcal C and Pneumovax vaccines, annual flu vaccination and COVID vaccinations as per high risk patients, all women should be offered hepatitis B vaccination if not already up to date)
- Serology for hepatitis viruses, HIV and immunity to rubella.
- Red cell antibody status,
- Echocardiogram (if not performed within the last year or if symptomatic) and lung function tests
- Assessment of renal function: Blood pressure monitoring, U&Es and Urinalysis (for both proteinuria and microalbuminuria).

Discussion regarding any co-existent medical conditions Endocrinopathies, renal dysfunction, restrictive lung defect, pulmonary hypertension are complications that may have an impact on pregnancy and anaesthetic risks of the patient.

Antenatal Management

Pregnant women from Bristol and Weston with a sickle cell disorder should be managed at St. Michael's hospital as the Bristol Haematology Unit at BHOC is a sickle cell disease specialist centre, is in close proximity and has appropriate expertise. Women who live out of area can be managed at their local centre with discussion in the Regional Obstetric Haematology MDT. Please refer to South West Maternal Medicine Network via refer-a-patient.

A joint care plan should be agreed for all patients and be carried in their hand-held maternity notes.

Booking Procedure for women with sickle cell disease

Women should be seen in the Obstetric Medicine/Haematology ANC, preferably by 8 -10 weeks gestation. A letter of referral is required from the General Practitioner (submitted via the eRS system) or from the Haematologist directly to the maternal medicine team with information regarding their condition. This should not delay an early booking appointment.

In addition to normal booking procedure, the following should be undertaken:

History for women with sickle cell disease:

- Frequency and nature of sickle crises
- Acute and chronic complications
- Transfusion history
- Infections
- Preferred options in the management of their SCD including history of allergies, choice of analgesics etc.

Examination for women with sickle cell disease:

- Physical examination
- Oxygen saturation
- > Consider echocardiogram/ retinal screening if appropriate

Investigations for women with sickle cell disease:

- Routine booking bloods
- ➢ FBC
- > Haemoglobin electrophoresis and HbS concentration
- Red cell, serum folate, ferritin
- U&Es, LFTs
- CMV status (+ HIV/Hep C if not done)
- > Red cell genotype and extended blood group antibody screen (Haematology to facilitate)
- Urine microscopy and culture (MSU) performed monthly
- ECHO and lung function tests

Management of women with sickle cell disease

- Arrangements for partner testing should be made (if not done). If their partner has a haemoglobin disorder that could result in the child having sickle cell disease, counselling should take place in the first trimester with offer of prenatal diagnosis. If the fetus is affected, the option of termination should be offered.
- > Folic acid 5mg od should be prescribed (if not already commenced prenatally)
- Penicillin V 250mg twice daily (or erythromycin 500mg twice daily if penicillin allergic): SCD is associated with hyposplenism.
- Consider low-dose Aspirin (150mg daily from 12/40 to 36/40) due to increased risk of preeclampsia
- A VTE risk assessment should be undertaken at booking and regularly throughout pregnancy. Offer prophylactic anticoagulation if additional risk factors at booking or at 28 weeks if no additional risk factors.
- ➢ Iron supplementation should be given if proven iron deficiency (ferritin ≤ 30); it should not be given empirically as for anaemic women without haemoglobinopathy
- Consider effects of any other medications (i.e. NSAIDs/opioids) and suggest alternatives and agree a pain management plan for the treatment of acute painful crisis.
- Arrange dating ultrasound scan
- Explain risks of pregnancy (see under pre-pregnancy counselling above) and make an individualised management plan for antenatal care.
- Women with persistent vomiting should be advised to seek medical advice early and may require admission to maintain hydration to reduce the risk of a sickle cell crisis.
- Discuss suitable positions for delivery with women who have hip replacements (secondary to avascular necrosis).
- Mark notes clearly with sickle cell disorder e.g. HbSS (sickle cell anaemia), HbSC disorder, Sickle beta thalassaemia, HbSD disorder, HbSE disorder

Subsequent Antenatal management for women with sickle cell disease:

The woman should be seen in conjunction with the consultant haematologist in the haematology clinic/ joint obstetric haematology clinic. See appendix for detailed schedule

Follow up will be determined by the individual management plan and will normally be:

- Monthly until 24-28 weeks
- > Fortnightly intervals until 32-36 weeks (dependent on maternal/ fetal condition)
- Weekly until term

Monitor for potential maternal and fetal complications:

- > Maternal anaemia a patient specific minimum Hb level should be set
- Increased risk of infection which may precipitate a crisis
- Asymptomatic urine infection
- Hypertension and pre-eclampsia
- Thromboembolic disease
- Increased miscarriage risk
- Fetal growth restriction
- Prematurity and stillbirth
- Increased risk of placental abruption
- If the baby will potentially be affected by a haemoglobin disorder the Paediatric Haemoglobinopathy team should be alerted to the pregnancy.

Investigations:

See appendix for clinic schedule which should be printed off and filed in the handheld antenatal notes

Continue to explain the proposed plan of management to the woman and ask her to report promptly any signs of infections or impending sickle cell crises.

An individualised management plan for labour and the post-partum period will be written in conjunction with the woman and the multidisciplinary team. This will take into account her previous sickle and pregnancy history and will be documented in the handheld notes, on the maternal medicine workspace and in the high-risk pregnancy file on central Delivery Suite. It should be reviewed and updated at every clinic appointment.

Specific Management for women with sickle cell disease

1. Sickle Cell Crises

If hospital admission is necessary, the patient should be admitted to Ward D703 BHOC Tel No: . Within hours, please liaise with the Haemoglobinopathy CNS team

or mobile . The Haematologist will contact the Obstetrician to discuss further management. For guidance, refer to

The patient will require:

- Adequate analgesia (NSAIDS are best avoided in pregnancy and are contraindicated before 14 and after 32 weeks gestation).
- Rehydration
- Oxygenation
- Treatment of associated complications (e.g. infection)

VTE prophylaxis dose according to weight

Investigation :

- ➢ FBC, HbS quantitation, U+E's, LFT's.
- Check precipitating cause of possible infection by blood culture and MSU, treat with appropriate antibiotics.
- Respiratory investigations Oxygen saturation If there is impairment CXR, arterial blood gases
- Monitor fetal wellbeing by CTG (if >28 weeks gestation).

The pregnant woman should be assessed by both the haematology and obstetric teams prior to discharge.

Other acute presentations

- Acute stroke should be considered in women presenting with acute neurological impairment and requires urgent consideration of exchange transfusion.
- Acute erythrovirus infection (parovirus B19) should be considered in women presenting with acute anaemia, this is usually associated with reticulocytopenia and may be accompanied by neutropenia and thrombocytopenia.

3. Hypertensive Disease

Both severe pregnancy induced hypertensive disease, and underlying renal hypertension due to recurrent sickling and damage to the kidneys, may occur. The management is the same as the usual obstetric management of hypertensive disorders see

3. Infections

SCD is associated with hyposplenism and increased risk of infection. Infection occurs in 50% of pregnant women with SCD (mostly UTI and respiratory).

- Treat all confirmed infections promptly and aggressively with antibiotics as indicated in UH Bristol and Weston antibiotic guideline.
- If an infection i.e UTI is suspected, but not yet confirmed, treat with a broad-spectrum antibiotic until the MSU result is available.
- Any pyrexia warrants an infection screen and commencement of broad-spectrum antibiotics. The subsequent results of the screen will determine continuation or discontinuation of antibiotics.
- There should be a low threshold for admission to maintain warmth, hydration, and oxygenation.

4. Indications for transfusion

Each woman will be considered on an individual basis by the obstetrician and haematologist and a minimum Hb level at which transfusion should be recommended, determined, and recorded in the management plan.

Women receiving long-term transfusion for stroke prevention or amelioration of severe sickle complications should continue with regular transfusion throughout pregnancy.



The risks and benefits of prophylactic transfusion during pregnancy should be discussed with the patient as part of the haematology/obstetric consultation. Prophylactic transfusion is not routinely recommended but should be considered for women with:

- > Previous or current medical, obstetric, or fetal problems related to SCD
- Women previously on hydroxycarbamide due to severe disease
- Multiple pregnancy

Acute transfusion should be considered in the following situations:

- ➢ Hb<60g/dl</p>
- > Anaemia with cardio or respiratory compromise
- > Acute SCD complications (stroke, repeated crises, acute chest syndromes)

If indicated, transfusion should be given under the direction of the haematology team to maintain the HbS level<30% and a target Hb of 100-110g/dl. Blood may be given by exchange and/or top-up. Full HbS-negative and extended Rh- and Kell-matched CMV-negative (in non-immune individuals) red cells should be used. If there are clinically significant red cell antibodies (current or historical) then the red cells should be negative for the corresponding antigens.

Anticoagulation policy

SCD is a major risk factor for VTE in pregnancy.

All women with SCD should have a VTE risk assessment performed and clearly documented in early pregnancy, at 28 weeks, in the intrapartum and early postpartum periods and if admitted to hospital.

Prophylactic low molecular weight heparin (LMWH) is recommended from booking if additional risk factors for VTE are present, and if a woman is admitted to hospital (should be continued throughout admission). In women without additional risk factors it should also be considered from 28 weeks of pregnancy and up to 6 weeks postpartum.

Anaesthetic considerations

An anaesthetic review should be performed in the third trimester to discuss analgesic/anaesthesia options in labour and the postpartum period. Opioids may be used except for pethidine (risk of seizures with SCD). Epidural anaesthesia is safe and effective. Regional anaesthetic is recommended for caesarean section (additional risks of general anaesthesia with SCD).

Review venous access and consider placement of a midline/PICC to facilitate management if concerns.

Women are at high risk of sickle cell crises around the time of delivery, patient-controlled analgesia has been shown to be highly effective in managing sickle pain and there should be a low threshold to use this if women are describing sickle pain that is not controlled with simple analgesia.

Cell salvage is contraindicated in women with sickle cell disorders. For women with sickle cell trait

cell salvage can be considered.

Labour and Delivery for women with sickle cell disease

Unless there are any specific complications, a normal vaginal delivery can be anticipated.

There is evidence that placental function deteriorates after term gestation and so induction of labour after 38 weeks should be considered in all women with SCD who have a normally grown baby.

An individual plan will be available in the patient's handheld notes, on the maternal medicine workspace and in the Central Delivery Suite high risk pregnancy file.

NB – Women with sickling pain will not always present in the same way as other patients in severe pain, ie to the observer they may not behave in a way that suggests severe pain. This is in part because they often have chronic pain with acute exacerbations. They will usually recognise their sickling pain distinct from other pains.

Sometimes these episodes require high levels of opioid analgesia and because of their past use of opioids to control pain they may require bigger and more frequent doses than would be expected in other patients.

As a group they frequently report delays in receiving adequate pain relief and that health care professionals unfamiliar with their underlying condition unfairly label them as exhibiting inappropriate opioid seeking behaviours. Pain relief should be delivered promptly and without judgement. There should be a low threshold for patient-controlled analgesia (PCA) which is the standard of care in severe sickle cell crises.

On Admission for Delivery for women with sickle cell disease

The patient should be admitted to St. Michael's Hospital Central Delivery Suite. The senior midwife, maternal medicine obstetrician, anaesthetist and paediatrician should be informed at the earliest opportunity. The on-call Haematology team should be contacted if there are any concerns over sickle complications.

- Routine observations.
- Bloods FBC, group and save (consider crossmatched blood if atypical antibodies present)
- Observe for signs of infection.
- Keep patient warm and well hydrated
- Ensure venous access
- Monitor O2 sats and give O2 via a facial mask if <95%</p>
- Monitor fluid balance carefully with strict fluid balance charts for all women in labour. The aim is to avoid dehydration which can trigger a sickle crisis without causing fluid overload. Intravenous fluids may be required to maintain adequate hydration. If pre-eclampsia is present fluid balance will be more challenging. It is recommended that oxygen saturation monitoring is commenced. The amount of rehydration will need to be decided between obstetrician and anaesthetist with a lower threshold for CVP monitoring than in women without SCD



- IV antibiotics should be given at an early stage if there is a maternal pyrexia, tachycardia or prolonged rupture of membranes.
- Continuous intrapartum CTG monitoring is recommended.
- Active management of the third stage is recommended to reduce blood loss.

NB. Avoid

- > Dehydration
- > Sepsis
- Maternal hypoxia or excessively prolonged labour
- Pethidine risk of toxicity and pethidine-associated seizures

Caesarean Section for women with sickle cell disease (elective or emergency)

(See also

- > Ensure adequate hydration and oxygenation
- > Wherever possible, use of regional analgesia is preferred
- Antibiotic prophylaxis should be given
- > Postpartum maintain on hourly observations (HDU chart) for first 8 hours.
- If O2 sats fall below 92% (despite face mask/rebreathing bag oxygen), then CPAP may be necessary

Postnatal management

- Low threshold for keeping on central delivery suite especially if concerns over sickle pain as may need PCA
- > Continue with prophylactic medication, penicillin and folic acid.
- > 6 weeks of LMWH should be given routinely for VTE prophylaxis
- > Maintain good hydration (low threshold for IV fluids) and oxygenation for first 24 hours.
- Encourage breast feeding.
- Encourage early mobilisation
- If there are any haematological concerns about the baby, then the neonatologists and oncall paediatric haematologists should be informed.

Women should be advised that they have an increased risk of pain episodes in the postnatal period and precipitants should be avoided

NB: Patient is most at risk of sickle related complications for the first few days after delivery. Infection and lack of good hydration are the main precursors.

Newborn Screening

Babies at high risk of SCD, (i.e. paternal testing confirmed presence of a relevant haemoglobinopathy) should be tested via a capillary blood sample taken soon after birth. Arrangements should be in place to communicate the result to the mother as soon as possible and refer to the Paediatric Haemoglobinopathy service.

Contraception for women with sickle cell disease

Women and their primary care team should be provided with full information about all methods of contraception available, discussing advantages and disadvantages.

Advise the contraceptive that is appropriate for the individual woman's needs:

- Progesterone-only contraceptives such as the progesterone only pill, injectable contraceptives, implants and IUS (e.g. Mirena) are safe and effective in women with SCD (FSRH Category 1 unrestricted use). There is some evidence for reduction in sickle cell pain associated with progesterone-only preparations.
- The combined oral contraceptive pill has a theoretical increased risk of thrombosis/sickle cell crisis. If used for women with SCD, cardiovascular risk factors should be minimised to mitigate risk. (FSRH Category 2 – advantages outweigh theoretical risks).
- IUCD (intrauterine contraceptive device) has a potential increased risk of blood loss (FSRH Category 2 – advantages outweigh theoretical risks), so the IUS is the preferred option.

Discharge for women with sickle cell disease

- Ensure patient has sufficient medication: analgesia, folic acid, penicillin, enoxaparin (6 weeks).
- Ensure they have been taught to administer enoxaparin
- Make outpatient appointment for them to be reviewed by the Haemoglobinopathy team postnatally - this is likely to be initially by telephone.

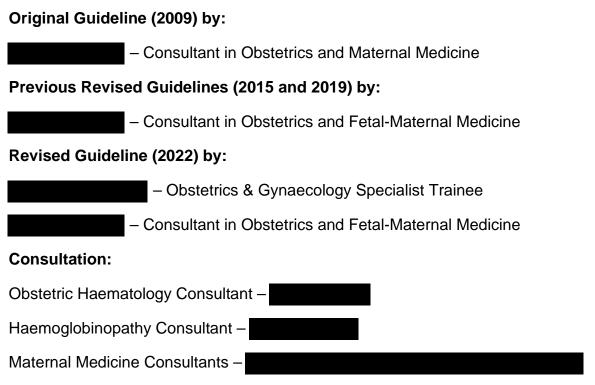
	mobile

Email:

- All babies will be tested for sickle cell disease on the heel prick test and if a diagnosis confirmed this will automatically be registered on NHR and the haemoglobinopathy team will be automatically notified
- If any concerns about the baby, please discuss with Paediatric Haematology; ask for the Benign Paediatric Haematologist via switchboard

General Advice for women with sickle cell disease

- Drink at least 3 to 4 litres of fluid a day.
- Comply with taking medications prescribed.
- ➢ Keep warm.
- Avoid over exertion.
- Eat a well-balanced diet.
- Keep clinic appointments.
- > Contact GP or the Bristol Haematology Unit at BHOC if they feel unwell.



Sickle Cell and Thalassaemia Clinical Coordinator

Table A	
REFERENCES	 S. Pavord, B. Hunt. The Obstetric Haematology Manual. Second Edition. Cambridge University Press. 2018 Management of Sickle Cell Disease in Pregnancy. Green-top Guideline No. 61. Royal College of Obstetricians and Gynaecologists. July 2011 Standards for the Clinical Care of Adults with Sickle Cell disease in the UK. Sickle cell society 2018 E. Oteng-Ntim et al. Management of Sickle Cell Disease in Pregnancy. A British Society for Haematology Guideline 2021
RELATED DOCUMENTS AND PAGES	Transfusion in sickle cell disease DMS address: Perioperative management of SCD Thromboprophylaxis in pregnancy, labour and postnatal period
AUTHORISING BODY	Antenatal Working Party
SAFETY	
QUERIES AND CONTACT	Contact: , Consultants in Maternal Medicine, St Michael's Hospital
AUDIT REQUIREMENTS /STANDARDS	 All pregnant woman with SCD should be offered partner screening and, if her partner is a carrier, early counselling, first-trimester diagnosis and a discussion of the options; target 100%. Women with SCD who are attempting to conceive should not be taking hydroxycarbamide, unless the woman is considered to be at high risk of serious complications and blood transfusion is not feasible; target 0%. Women with SCD who are attempting to conceive should not be taking ACE inhibitors; target 0%. Women should receive antenatal care from a multidisciplinary team including an obstetrician and midwife with experience of high-risk antenatal care and a haematologist with links to a specialised haemoglobinopathy team; target 100%. All women with SCD who are planning pregnancy should be offered folic acid 5 mg once daily (od) and this should be continued throughout pregnancy; target 100%. Women with SCD should be offered penicillin V 250 mg twice daily (bd) or an alternative throughout pregnancy; target 100%. Women with SCD should be prescribed prophylactic low-molecular-weight heparin (LMWH) from 28 weeks gestation or from presentation of pregnancy if there were additional risk factors; target 100%. All women with SCD were prescribed prophylactic LMWH for six weeks after

Clinic schedule for women with sickle cell disorders Please print off and file in the handheld pregnancy notes

	Please print off and file in the handheld pregnancy notes	
Appointment	Actions Circle any actions that could not be completed and document in antenatal notes that there is an outstanding action	Sign
First appointment Obs Haem clinic	Information, education and advice about SCD and pregnancy Review results of father's haemoglobinopathy screen if available and discuss PND if appropriate OR Offer partner testing if not already done	
	Clinical history to assess SCD complications in particular assess and document any retinal, renal or cardiac complications	
	Review medications and individual pain management plan Ensure women are taking 5mg folic acid & prophylactic antibiotics & discuss vaccinations	
	Extended red cell phenotype if not previously performed (Haemoglobinopathy team can arrange if needed)	
	Prescribe 150 mg aspirin Document baseline oxygen saturations and blood pressure	
<u> </u>	Send MSU for culture Plan and book fetal growth scans/Dopplers	
Booking appointment	Offer general health information, advice and support. Review results of father's haemoglobinopathy screen and discuss PND if appropriate. Baseline full blood count, renal function test, urine protein/creatinine ratio, liver function test, ferritin	
(Midwife)	and group and screen Start vitamin D prophylaxis if not already on this	
	Risk assessment for VTE and consider thromboprophylaxis Please note all women should follow the primip pathway for appointments and will need an	
11+²-14 weeks USS	additional community midwife appointment at 39 weeks if not delivered First-trimester ultrasound scan (booked by midwife)	
16 weeks	Routine midwife appointment – BP & Urinalysis*	
Midwife Obs Haem ANC	Review by consultant obstetrician and haematologist repeat MSU	
20 weeks USS	Routine anomaly scan (booked by midwife) Review by consultant obstetrician and haematologist	
Obs Haem ANC	repeat FBC and MSU	
24 weeks Obs Haem ANC & USS	Ultrasound monitoring of fetal growth and amniotic fluid volume (booked by Obs Haem) Repeat FBC and MSU	
25 weeks Midwife	Routine appointment - BP/urinalysis*	
28 weeks Midwife Obs Haem ANC &	Routine appointment for FBC and antenatal grouping +/- administer anti-D if indicated Ultrasound monitoring of fetal growth and amniotic fluid volume (booked by Obs Haem) Repeat MSU	
USS 31 weeks	Review VTE risk factors and consider thromboprophylaxis	
Midwife	Routine midwife appointment including multips – BP/urinalysis*	
32 weeks Obs Haem ANC & USS	Ultrasound monitoring of fetal growth and amniotic fluid volume (booked by Obs Haem) Repeat MSU and FBC Offer anaesthetic assessment at 32 weeks or earlier if indicated	
34 weeks		
Midwife	Routine midwife appointment – BP/urinalysis*	
36 weeks Obs Haem ANC & USS	Ultrasound monitoring of fetal growth and amniotic fluid volume Routine check – BP & Urinalysis Repeat MSU and FBC	
	Consider whether to stop aspirin prior to delivery Offer information and advice about: Timing, mode and management of the birth Care of baby after birth Analgesia and anaesthesia	
38 weeks Midwife	Routine midwife appointment check – BP & Urinalysis*	
39 weeks Midwife	Midwife appointment NB not part of routine schedule BP & Urinalysis*	
40 weeks Obs Haem ANC	Review by obstetrician and offer fetal monitoring if woman declines delivery	

* Please discuss any abnormal BP or urinalysis results or any clinical concerns with the maternal medicine midwife/team at St Michaels promptly