Acute medical problems in pregnancy

ABSTRACT

The maternal population in the UK has become an increasingly challenging group of patients to manage. Women with pre-existing and often complex medical conditions are successfully conceiving. Most physicians will have had some involvement in the care of obstetric patients admitted with medical problems, and a lack of experience and fear of causing harm may result in essential investigations and treatment being withheld.

The physiological changes in pregnancy can complicate the interpretation of observations and test results. This article discusses the presentation of commonly encountered medical problems in the obstetric population, including breathlessness, chest pain, palpitations, seizure and headache. It covers specific investigations and suggested treatment in this subset of patients. These women should receive the same level of care and attention as those who are not pregnant. Early diagnosis and effective management can help to reduce maternal morbidity and mortality caused by medical problems arising during pregnancy.

The pregnant population in the UK has changed. Over the last four decades the average age to become a new parent has risen by 4 years to 30 years for women and 33 years for men (Haines, 2016). Obstetricians are increasingly managing older women with pre-existing and complex medical conditions, in addition to seeing de novo medical problems unmasked during the physiological changes of pregnancy. This has created a more challenging obstetric environment and one in which clinicians are having to rapidly adapt to anticipate medical complications and safely manage women with multiple comorbidities.

The 2017 MBRRACE-UK report showed that two thirds of women who died between 2013 and 2015 had pre-existing physical or mental health problems. Cardiac disease and venous thromboembolism continue to be leading causes of maternal mortality (Knight et al, 2017). Early investigation and treatment could help prevent these women from dying and it is essential that clinicians managing these patients do not withhold essential investigations and life-saving treatment because of the pregnancy.

This article provides an overview of common acute medical problems in pregnancy and how to investigate, diagnose and manage these appropriately.

Breathlessness

Breathlessness in pregnancy is very common and may not be pathological. Physiological breathlessness in pregnancy typically occurs in the last trimester, although it may occur at any point, and may be more noticeable at rest or when talking. It is caused by an increased awareness of the increase in minute ventilation. In addition, the gravid uterus splints the diaphragm towards term, impeding functional residual capacity. Importantly, respiratory rate, peak expiratory flow rate and forced expiratory volume in 1 second (FEV_1) do not change (*Table 1*).

Table 1. Physiological changes in respiratory markers in pregnancy

Respiratory markers	Changes in pregnancy
Respiratory rate	No change
Resting minute ventilation	Increases by up to 50%
Tidal volume	Increases
Functional residual capacity	Reduced in third trimester
Forced expiratory volume over 1 second, peak expiratory flow rate	No change
Blood gas analysis	Mild respiratory alkalosis

From Nelson-Piercy (2015)

Shortness of breath is a common presentation and has many other causes including infection, pulmonary embolus, asthma, spontaneous or traumatic pneumothorax, anaemia and cardiac causes. A thorough history and examination with observations and basic investigations – an electrocardiogram, blood tests and a chest X-ray – can help to differentiate these causes.

Pulmonary embolism and deep vein thrombosis

Venous thromboembolism is the leading direct cause of maternal morbidity in the UK (Knight et al, 2017). Diagnosis of venous thromboembolism is complicated because symptoms of breathlessness and limb swelling are common manifestations of a normal pregnancy. D-dimers and Wells scoring (a pre-test probability assessment for venous thromboembolism) are not validated in pregnancy. However, pregnant women are at greater risk of venous thromboembolism, particularly in the puerperium (*Table 2*). Symptoms can include leg pain and swelling

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Table 2. Risk factors for venous thromboembolism

Non-modifiable	Age >35 years
	Previous venous thromboembolism
	Family history of venous thromboembolism
	Heritable or acquire thrombophilia
	Parity ⩾3
	Medical comorbidities
	Pregnancy
Modifiable	Smoking
	Obesity (body mass index >30 kg/m^2)
	Dehydration
	Long-distance travel
	Assisted reproductive techniques
	Infection
	Hospitalization

From Royal College of Obstetricians and Gynaecologists (2015)

(usually unilateral) or lower abdominal pain if deep vein thrombosis has extended proximally. Breathlessness, chest pain, haemoptysis and collapse can occur with a pulmonary embolism. There can be a low-grade pyrexia and leucocytosis with venous thromboembolism (Royal College of Obstetricians and Gynaecologists, 2015).

Current guidelines recommend that if a clinical suspicion of venous thromboembolism exists, treatment with low molecular weight heparin is safe in pregnancy and can be commenced pending confirmation of diagnosis (Royal College of Obstetricians and Gynaecologists, 2015). Appropriate imaging includes ultrasound Doppler if clinical signs of deep vein thrombosis are present such as unilateral leg swelling. If a pulmonary embolism is suspected, a chest X-ray should be performed first to check for other causes of breathlessness. Failing an alternative diagnosis or if highly suspicious of a pulmonary embolism the patient should go on to have either a ventilation–perfusion scan or computed tomography pulmonary angiogram.

It is important to discuss the radiation risks of imaging *vs* establishing a diagnosis and further treatment. The Royal College of Obstetricians and Gynaecologists (2015) green-top guidelines no. 37b 'Thromboembolic Disease in Pregnancy and the Puerperium: Acute Management' recommend that women be advised that a ventilation–perfusion scan carries a slightly increased risk to the fetus of childhood cancer but that computed tomography pulmonary angiogram has a higher risk of maternal breast cancer. Both these absolute risks are very small (Royal College of Obstetricians and Gynaecologists, 2015). There may be no option for a nuclear medicine scan in the hospital, so local trust protocol should be followed accordingly.

In those with confirmed venous thromboembolism, low molecular weight heparin dosing should be titrated to the booking or pre-pregnancy weight of the patient. Pregnant women with confirmed venous thromboembolism should be treated for the entire course of their pregnancy through to 6 weeks post-partum. Treatment should be for a minimum of 3 months so late diagnosis will be treated beyond the 6 weeks post-partum period. Those considered very high risk for further venous thromboembolism may require a longer course of anticoagulation. An advance plan for the peripartum period and labour should be made with the anaesthetic and obstetric teams. Importantly, thrombolysis is not contraindicated in pregnancy should a patient present with massive life-threatening or submassive pulmonary embolism.

Respiratory infections

Co-existing asthma, smoking, immunosuppression and anaemia may increase the risk of pneumonia in pregnant women (Goodnight and Soper, 2005). Maternal complications of pneumonia include respiratory failure, and neonatal complications include pre-term birth and low birth weight. The most common pathogens affecting pregnant women include *Streptococcus pneumoniae*, *Haemophilus influenzae* and mycoplasma. Macrolides (clarithromycin and erythromycin) and beta-lactam antibiotics (cephalosporins, penicillin and carbapenems) are effective for most cases of community-acquired pneumonia in pregnancy and are considered safe.

Influenza can cause a variety of symptoms including myalgia, coryzal symptoms, cough, fever, headache, anorexia, and gastrointestinal disturbance such as abdominal pain or diarrhoea. Secondary bacterial infection from pathogens such as *S. pneumoniae*, Haemophilus and *Staphylococcus aureus* requires prompt antibiotic treatment and early admission to hospital if systemically unwell.

Pregnant women with influenza are more likely to be hospitalized than non-pregnant women and evidence from the H1N1 influenza pandemic in 2009 suggested that pregnant women were particularly vulnerable to severe infections and sepsis, resulting in increased maternal and neonatal mortality (Knight et al, 2017). A systematic review did not find increased mortality among pregnant women with influenza (Mertz et al, 2017) but the advice is to encourage all pregnant women to have the influenza vaccination. Women who were not vaccinated against influenza have an increased association with preterm labour and low birth weight babies (Nunes et al, 2016). Data on safety of oseltamivir (Tamiflu) in pregnancy are limited, but the National Institute for Health and Care Excellence recommends its use in influenza-positive patients.

Asthma

Asthma is the most common chronic disease in pregnancy and is prevalent in approximately 4–12% of the pregnant population (Goldie and Brightling, 2013). Asthma has the potential to improve or worsen during pregnancy. Good asthma control before and during pregnancy will reduce the risk of complications to both mother and fetus. It is important to continue usual asthma medications during and after pregnancy, even if breast feeding. Smoking cessation must be strongly encouraged. Medications including short- and long-acting beta agonists, inhaled corticosteroids and oral or intravenous theophylline, and leukotriene receptor antagonists should be used as normal during pregnancy to achieve optimal asthma control. Oral steroids should never be withheld because of pregnancy (British Thoracic Society, 2014).

Acute asthma management is the same as for a non-pregnant woman, including systemic steroids and magnesium sulphate. There should be a low threshold to refer to critical care if the patient is failing to respond adequately to initial treatment. It is important to look for precipitating causes for the asthma flare and check for pneumonia and pneumothorax on a chest X-ray.

Pneumothorax

A pneumothorax typically presents as sudden-onset pleuritic pain and breathlessness and can occur after a spontaneous vaginal delivery. Subcutaneous emphysema may be present. Management of tension, primary or secondary pneumothorax is the same as for non-pregnant patients.

Anaemia

Anaemia is common in pregnancy and can cause breathlessness. Anaemia is classified as a haemoglobin level <110 g/litre in the first trimester, <105 g/litre in the second trimester and <100 g/litre in the third trimester and post-partum (Pavord et al, 2012). The most common cause is iron deficiency anaemia. The British Society of Haematology 'UK guidelines on the management of iron deficiency in pregnancy in women with confirmed iron deficiency anaemia' recommend an initial trial of 100–200 mg daily oral iron but failing this parenteral iron infusion can be administered (Pavord et al, 2012). Blood transfusion should be reserved for life-threatening anaemia.

Cardiomyopathy

Peripartum cardiomyopathy is a condition specific to pregnancy. It occurs near term and post-partum and is characterized by left ventricular systolic dysfunction on echocardiography (ejection fraction <45%) and where no other cause of heart failure is found (Sliwa et al, 2010). Risk factors include increasing maternal age, black African or Caribbean ethnicity, multiple pregnancies and hypertension. Women can present with breathlessness, palpitations, peripheral oedema and reduced exercise tolerance. Elevated heart rate and respiratory rate, abnormal cardiac rhythms and signs of congestive cardiac failure or pulmonary oedema may be evident.

Treatment can include cardioselective beta-blockers, digoxin, diuretics, vasodilators (e.g. nitrates) and thromboprophylaxis. After delivery, angiotensin-converting enzymes inhibitors can be given (Nelson-Piercy, 2015). These women can be very sick and in extreme cases early discussion with the nearest cardiothoracic or extracorporeal membrane oxygenation centre is advised for further support such as intra-aortic balloon pumps, extracorporeal membrane oxygenation or left ventricular assist device until a heart transplant is available. As a minimum standard, these patients should be managed in the coronary care unit with regular input from the obstetric team.

Chest pain

There are many causes of chest pain, some of which have been discussed in the breathlessness section. As with any patient presenting with chest pain, a thorough history including a review of risk factors, clinical examination, electrocardiogram and chest X-ray may help narrow down the differential diagnosis.

Gastro-oesophageal reflux disease

Gastro-oesophageal reflux disease typically presents with retrosternal burning chest pain with associated acid brash, which is worse when lying flat (often noticed at night). It is more common towards the end of pregnancy because the gravid uterus splints the diaphragm. Antacids, omeprazole and ranitidine are safe to use in pregnancy and are usually effective.

Myocardial infarction and ischaemic heart disease

Cardiac disease is the leading cause of death in pregnancy in the UK (Knight et al, 2017). Myocardial infarction is a significant cause of maternal morbidity and mortality. The physiological changes of pregnancy can unmask underlying coronary artery disease by acting as 'nature's stress test' (Sanghavi and Rutherford, 2014). Increasing cardiac output and myocardial oxygen demand alongside relative anaemia and decreased diastolic blood pressure can exacerbate myocardial ischaemia (Wuntakal et al, 2013). Coronary artery dissection and thrombosis are relatively more common as causes of acute coronary syndrome in pregnancy.

Other risk factors for ischaemic heart disease are the same as those for the non-pregnant population, including pre-existing diabetes, hypertension, high cholesterol levels, family history and smoking.

All women with chest pain should have an electrocardiogram to look for ST elevation or dynamic changes on serial electrocardiograms. Troponin I or troponin T is sensitive to myocardial ischaemia and should be sent at the appropriate time. It is important to note that, unlike a D-dimer, troponin

Table 3. Differential diagnosis for seizure in pregnancy

Other causes of seizure	Distinguishing features
Eclampsia	Check for high blood pressure and proteinuria (but some women may have neither). Usually presents after 20 weeks' gestation. May have other symptoms including headaches, visual disturbance, epigastric pain, peripheral and/or facial oedema. This is a medical and obstetric emergency. Urgent blood pressure control and intravenous magnesium and obstetric high dependency care input
Thrombotic thrombocytopenic purpura	Fever, neurological and acute kidney injury, low platelets and haemolytic anaemia
Cerebrovascular accident	Persistent neurological impairment is usually present. Arrange an urgent computed tomography or magnetic resonance imaging of the head to look for haemorrhage or infarct. Early discussion and transfer to neurosurgical unit if the former and hyperacute stroke unit if the latter. Thrombolysis for the latter is not contraindicated and should be considered if symptoms are persisting or progressing. This should be discussed with the on-call stroke and obstetric consultant
Cerebral venous thrombosis	Arrange computed tomography venogram, anticoagulate with low molecular weight heparin
Hypoglycaemia	Treat the hypoglycaemia and re-assess to check if neurological symptoms resolve
Electrolyte imbalance	Check for low sodium and low calcium levels
Posterior reversible leukoencephalopathy syndrome	Magnetic resonance imaging of the head shows changes that usually resolve 1–2 weeks post-partum. Associated with high blood pressure and visual disturbance
Reversible cerebral vasoconstriction syndrome	Thunderclap headache with changes seen on magnetic resonance imaging angiography; usually presents post-partum and resolves within 3 weeks
Space-occupying lesion	Possible focal neurological deficit and evidence of space-occupying lesion on computed tomography or magnetic resonance imaging.

From Coad et al (2017)

is never increased above the upper limit of normal in healthy pregnancy (Wuntakal et al,). As with the non-pregnant population, do not wait for a troponin measurement if there is ST elevation. The patient needs urgent transfer to the catheterisation laboratory for assessment and primary percutaneous coronary intervention.

Treatment for non-ST elevation myocardial infarction should be with low-dose aspirin (75 mg), heparin and nitrates. Clopidogrel is safe but should be discontinued at least a week before delivery to allow for regional analgesia. Angiotensin-converting enzyme inhibitors, angiotensin-receptor blockers and statins are contraindicated in pregnancy but can be initiated post-partum. All women presenting with acute coronary syndrome need to be managed on a high dependency unit with close obstetric supervision and fetal monitoring. Where possible, delivery should be delayed for at least 2–3 weeks following a coronary event (Wuntakal et al,).

Aortic dissection

It is difficult to get a true measure of the incidence of aortic dissection in the pregnant population as a result of variable reporting (Banerjee et al, 2015) but the overall incidence is low (Nienaber et al, 2004). Pregnancy and delivery are independent risk factors for aortic dissection but this risk is compounded by poorly controlled hypertension, presence of a connective tissue disorder such as Marfan syndrome (Roman et al, 2016) and a bicuspid aortic valve (Bonow et al, 2008).

Aortic dissection typically occurs in the late third trimester or early post partum. Women present with a multitude of symptoms including 'tearing' chest pain radiating to the back, breathlessness, vomiting, collapse and cardiac arrest. A computed tomography aortogram can assess whether the dissection involves the ascending aorta (type A – a surgical emergency) or is distal to the left subclavian artery (type B – rare in pregnancy). Careful management of hypertension and urgent discussion with cardiothoracic surgeons for type A dissection is the mainstay of treatment aside from supportive care.

Palpitations

During pregnancy a woman's heart rate may increase by 10–20 beats per minute and physiological palpitations may be present. However, it is important to exclude pathological causes of palpitations including hyperthyroidism, pulmonary embolism, arrhythmias, hypovolaemia and sepsis (Nelson-Piercy, 2015).

An electrocardiogram and 24-hour Holter monitor should be arranged if palpitations are concerning – and in the presence of an abnormal rhythm, an echocardiogram should be requested to look for structural heart disease.

Paroxysmal supraventricular tachycardia is the commonest arrhythmia encountered during pregnancy and can increase in frequency in women with pre-existing supraventricular tachycardia. It can present with breathlessness, palpitations, dizziness, presyncope or syncope. Supraventricular tachycardias are often self-terminating, but adenosine can be given to terminate an event or reveal the underlying rhythm. Beta-blockers or calcium-channel blockers (verapamil) and flecainide can be used (Nelson-Piercy, 2015) to manage palpitations.

Seizure

There are many causes for seizures in pregnancy as listed in *Table 3*. This review will focus on the management of epileptic seizures, but it is important to consider these other causes and to treat them appropriately.

Table 4. Red flag signs and symptoms for headaches

History	New onset severe headache
	Abnormal headache compared to usual
	Increasing frequency of headaches
	Nausea and vomiting
	Visual disturbance
	Thunderclap headache
Examination	Neck stiffness
	Photophobia
	Optic disc swelling on ophthalmoscopy
	Focal neurological signs
	Hypertensive
	Fever
	Altered Glasgow Coma Score and/or seizure activity

From Schoen et al (2015)

Epilepsy

Epilepsy affects 0.5–1% of women of child-bearing age and is the commonest neurological disorder seen in pregnancy (Edey et al, 2014). Sudden unexplained death in epilepsy remains the major cause of death in pregnant and post-partum women with epilepsy and is the third most common indirect cause of maternal mortality (Knight et al, 2017).

If a pregnant woman presents in status epilepticus she must be managed as a non-pregnant patient would be managed, with early airway protection and anaesthetic input, administration of antiepileptic drugs and escalation to critical care. Importantly, the patient must be seen by the obstetricians and neurologists before discharge home so that seizure management and delivery plans can be discussed.

More commonly, the acute medic will be involved in reviewing a post-seizure patient. It is important to consider why this patient has had seizures. Is she taking her medication? Is she on the correct dose? Is she abusing drugs and alcohol? Has she got an infection?

Owing to increased plasma volume and drug clearance, lamotrigine and levetiracetam usually require dose increases during pregnancy. Any change in medication or suggestion about discontinuation of an antiepileptic drug must be carefully discussed between the patient and neurologist. Five of the nine women who died from epilepsy in the UK between 2013 and 2015 had stopped their medication, contributing to poor seizure control and increased risk of sudden unexplained death in epilepsy (Knight et al, 2017). Green-top guidelines from the Royal College of Obstetricians and Gynaecologists (2016) advocate both written and verbal information about the risks and benefits of antiepileptic drugs for all women considering pregnancy. If a woman presents to hospital with an unplanned pregnancy, she must not stop her antiepileptic drug abruptly, but be urgently referred to a joint epilepsy–obstetric clinic for review.

"If a pregnant woman presents in status epilepticus she must be managed as a non-pregnant patient would be managed."

Headache

Headache is a common reason for pregnant women to present to their family doctor, the emergency department or ambulatory care. Migraine and tension headache are the most common diagnoses but it is important to be vigilant for other more serious aetiology and check for 'red flag' signs and symptoms (*Table 4*). It is important to be aware of drug-induced headache from vasodilators and calcium-channel antagonists (nifedipine), and postdural puncture headache, although these causes are not discussed here.

Migraine

Migraine is typically a throbbing, unilateral headache, made worse by movement, light and sound. These headaches may last hours to a few days and be associated with nausea and vomiting. Patients may report an aura, often visual symptoms (zigzag lines and flashes of light) and can have focal neurological signs including hemiplegia. Any ongoing neurological deficit should be investigated with neuroimaging.

The mainstay of treatment is avoiding triggers (poor sleep, stress, certain food and alcohol) and treating an acute attack with simple analgesia and an antiemetic. Non-steroidal anti-inflammatory medication can be given up to the third trimester. If a woman has more than two migraines per month, preventative medication should be considered, for example aspirin 75 mg daily or propranolol (Jarvis et al, 2018). Patients with persistent or difficult to manage migraines should be referred to a neurology clinic.

Subarachnoid haemorrhage

Subarachnoid haemorrhage is rare. The overall mortality rate of intracerebral haemorrhage between 2013 and 2015 was 0.48 per 100 000. Of the twelve women who died from an intracerebral bleed, seven were the result of subarachnoid haemorrhage. Symptoms of a subarachnoid haemorrhage include thunderclap headache, nausea and vomiting, seizures and focal neurological deficit.

Investigation includes a non-contrast computed tomography of the head and a lumbar puncture to look for xanthochromia. If the computed tomography scan of the head is performed within 6 hours of onset, it is highly sensitive in ruling out aneurysmal subarachnoid haemorrhage (Dubosh et al, 2016) and there may be

KEY POINTS

- The physiological changes of pregnancy can unmask new medical conditions and cause decompensation of pre-existing medical problems.
- Never assign symptoms to pregnancy alone without taking a thorough history and performing an examination.
- Investigations and medical treatment should not be withheld just because a patient is pregnant.
- Appropriate specialist follow up must be confirmed before discharging a patient from an acute admission.

no need to perform a lumbar puncture, although many clinicians will choose to carry out a lumbar puncture regardless. Women with a confirmed subarachnoid haemorrhage will need further computed tomography angiogram to look for an arteriovenous malformation or aneurysm. They need admission to hospital and urgent referral or transfer to a neurosurgical unit.

Cerebral venous thrombosis

The prothrombotic state of pregnancy increases a woman's risk of developing cerebral venous thrombosis, particularly in the third trimester and puerperium. The headache may typically be sub-acute in onset and associated with nausea and vomiting, focal neurological deficit and optic disc swelling suggestive of raised intracranial pressure. Magnetic resonance imaging and venogram are the imaging tools of choice to look for thrombosis. Women will need anticoagulation with heparin during pregnancy and the puerperium as for any venous thromboembolism.

Reversible cerebral vasoconstriction syndrome

This is an increasingly recognized syndrome that may present like a subarachnoid haemorrhage or transient ischaemic attack and is not unique to pregnant women. The predominant symptom is a posterior thunderclap headache radiating bilaterally and lasting 1–3 hours, often with up to four further episodes. Triggers can include sexual activity, emotional or stressful situations, and straining. It can be associated with vasoconstrictive medication such as ergot derivatives. Importantly, there are no new symptoms over the next few weeks and symptoms usually resolve after 3–4 weeks (Ducros, 2012). Diagnosis is made with computed tomography or magnetic resonance angiography and gives a beaded appearance of the intracerebral arteries where they are intermittently constricted. It is usually self-limiting but nimodipine can be used to ease symptoms.

Posterior reversible encephalopathy syndrome

This is typically a constant occipital headache unresponsive to analgesia and strongly associated with seizures and cortical blindness. In the pregnant patient it is associated with pre-eclampsia or eclampsia. It is thought to be caused by vasogenic brain oedema and gives a characteristic appearance of white-grey matter involvement bilaterally on magnetic resonance imaging. Symptoms can dramatically improve by lowering blood pressure and use of magnesium sulphate in the acute setting (Hobson et al, 2012).

Brief notes on other pregnancy-specific conditions

Acute fatty liver of pregnancy

This is a rare complication of pregnancy causing profound derangement of liver function. Women present with nausea and vomiting, anorexia, jaundice, abdominal pain, polyuria and polydipsia. Management of these women includes supportive care and early delivery of the fetus.

Haemolysis, elevated liver enzymes and low platelets (HELLP)

HELLP syndrome is a severe variant of pre-eclampsia. Patients with HELLP may present in a similar way to those with acute fatty liver of pregnancy with the addition of hypertension, although this is not always the case. Other causes of abdominal pain such as cholecystitis or liver haematoma should be excluded with imaging. Supportive care and prompt delivery is needed in these patients.

Hyperemesis gravidarum

Hyperemesis gravidarum occurs early in pregnancy, usually around 6–8 weeks, and usually self-terminates by about 20 weeks' gestation. Prolonged and protracted vomiting can cause severe dehydration, malnutrition and electrolyte disturbance. It can be associated with a slight rise in serum transaminase and bilirubin levels. Careful electrolyte replacement is required alongside antiemetics. It is important to avoid dextrose-containing infusions that could precipitate Wernicke's encephalopathy.

Conclusions

A diagnosis can often be made from the history and supported with examination findings and basic investigations. The added complexity of managing a pregnancy and the physiological changes associated with it make some diagnoses more difficult to reach, so having a basic understanding of haemodynamic changes associated with pregnancy is crucial. It is critical that pregnant women receive the same level of care and investigation as the non-pregnant population and that vital investigations and life-saving treatment are not withheld. BJHM

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