

Hyperemesis, gastro-intestinal and liver disorders in pregnancy

Clare Cuckson

Sarah Germain

Abstract

This review aims to discuss some of the common and serious conditions of the gastro-intestinal, hepatic and biliary tracts in pregnancy. Hyperemesis gravidarum is a condition which can lead to serious complications such as Wernicke's Encephalopathy. Hepatic disorders specific to pregnancy such as the HELLP syndrome (haemolysis, elevated liver enzymes and low platelets) and Acute Fatty Liver of Pregnancy (AFLP) are discussed. Management of Obstetric Cholestasis is also covered. Some forms of Hepatitis can be much more severe in pregnancy such as Herpes Simplex and Hepatitis E. The course of inflammatory bowel disease is generally unaffected by pregnancy and but flares should be managed as in the non-pregnant patient. Knowledge of the treatment options available and their safety in pregnancy is important to ensure these patients are adequately treated. Conditions such as appendicitis may have an atypical presentation in pregnancy and therefore diagnosis may be delayed.

Keywords AFLP; appendicitis; coeliac disease; Crohn's disease; HELLP; hepatitis; hyperemesis gravidarum; obstetric cholestasis; pancreatitis; pregnancy; ulcerative colitis

Physiological changes in pregnancy

During pregnancy there is generalized relaxation of smooth muscle resulting in relaxation of the oesophageal sphincter, reduced gastric peristalsis and delayed gastric emptying. Small and large bowel transit times are increased.

There is increased blood flow to the liver and increased production of fibrinogen, transferrin and many other binding proteins. Reference ranges for many liver function tests are altered. Gestation specific alkaline phosphatase is increased, mainly from increased placental production, and aminotransferases and gamma gluteryl transaminase are reduced.

Nausea, vomiting and hyperemesis gravidarum

Background: nausea is experienced by up to 90% of women during pregnancy and 50% complain of vomiting. Symptoms can

Clare Cuckson BA MB BChir MRCOG is a Specialist Registrar Obstetrics at Queen Charlotte's and Chelsea Hospital, London, UK. Conflicts of interest: none declared.

Sarah Germain MA MB BS DPhil MRCP is a Specialist Registrar in Obstetric Medicine/Diabetes and Endocrinology at Queen Charlotte's Hospital and St. Thomas' Hospital, London, UK. Conflicts of interest: none declared.

start from 5 weeks and usually resolve by the end of the first trimester. Persistent vomiting in pregnancy is termed hyperemesis gravidarum (HG) when the woman is unable to maintain adequate hydration and nutrition. The cause of HG is incompletely understood but hormonal, mechanical and psychological factors have been implicated. Biochemical thyrotoxicosis [raised free thyroxine and suppressed thyroid stimulating hormone (TSH)] is thought to occur by the stimulatory action of human chorionic gonadotrophin (hCG) on the thyroid (hCG shares a common α -subunit with TSH).

Features: signs of HG include weight loss, muscle wasting, ptalism (inability to swallow saliva resulting in spitting and drooling) tachycardia and postural hypotension. Biochemical findings may include hyponatraemia, hypokalaemia, abnormal thyroid function and liver function, and metabolic hypochlor-aemic alkalosis (loss of HCl from stomach).

Complications: if inadequately treated HG can lead to significant maternal and fetal morbidity.

Maternal

Severe **hyponatraemia** or its over rapid correction can lead to **central pontine myelinolysis** or osmotic myelinolysis (presents with confusion, horizontal gaze paralysis, and spastic quadriplegia).

Wernicke's Encephalopathy (Vitamin B1 deficiency) can occur in any condition of unbalanced nutrition which lasts for 2–3 weeks. This presents with a triad of confusion, ataxia and ophthalmoplegia. It carries a mortality of between 10% and 15%, and incomplete recovery can lead to Korsakoff's psychosis where the patient develops antero- and retro-grade amnesia and confabulation.

Thromboembolism is a risk due to dehydration and immobility in hospital.

Others include vitamin deficiencies and aspiration of vomitus.

Fetal

Severe HG (abnormal biochemistry and/or Wernicke's) can result in intra-uterine growth restriction (IUGR) or even intra-uterine death (IUD), but overall there are lower risks of miscarriage, stillbirth and pre-term delivery.

Diagnosis & investigations: it is a diagnosis of exclusion and other causes must be considered especially if the vomiting starts after the first trimester. The possible differential diagnoses of nausea and vomiting in pregnancy are given in [Table 1](#).

Management: a protocol for management of hyperemesis is given in [Table 2](#). It is important to give the patient adequate reassurance as to the safety of anti-emetics in pregnancy as poor compliance is a major reason for failure of treatment. Mild cases can be managed as day cases giving intravenous rehydration and anti-emetics, and continuing with buccal medication or suppositories then oral once vomiting is under control. It is usual to advise continuing regular anti-emetics for 7 days following admission to prevent a recurrence of symptoms. Intravenous thiamine (Pabrinex[®]) should be given to moderate to severe

Differential diagnosis and relevant investigations of nausea and vomiting in pregnancy

Urinary tract infection	MSU
Renal failure (Uraemia)	U & E's
Gastro-oesophageal reflux/ Gastritis/peptic ulcer disease/	<i>Helicobacter pylori</i> antibodies, Endoscopy, Try empirical proton- pump inhibitor
Bowel obstruction	Plain abdominal X-ray, (Ultrasound can detect bowel dilatation and bowel tumours)
Pancreatitis	Amylase, calcium, glucose Abdominal ultrasound, MRCP
Diabetic ketoacidosis	Glucose, U & E's, Urinalysis for ketones, Glucose tolerance test
Addison's disease	U & E's, early morning cortisol, short synacthen test
Hyperthyroidism	TFT's, TSH receptor antibodies
CNS pathology; vestibular disorders, cerebral tumours	Neurological examination, CT/ MRI brain

Table 1

Management of Hyperemesis gravidarum

Investigations

Urea and electrolytes, full blood count, liver function tests, thyroid function tests, calcium
Mid Stream Urine
Ultrasound scan pelvis

Intravenous fluids

1 L 0.9% normal saline with 20 mmol potassium chloride over 2 h
1 L 0.9% normal saline with 20 mmol potassium chloride over 4 h
Followed by
1 L 0.9% normal saline every 8 h with potassium replacement dependant on serum level

Vitamin supplements

Thiamine PO 50 mg TDS or 100 mg IV in 100 ml normal saline once weekly or
Pabrinex® (contains 250 mg Thiamine, Riboflavin, Pyridoxine, nicotinamide, and Vitamin C)

Anti-emetics

1st line: Cyclizine 50 mg PO/IM/IV TDS
2nd line: Metoclopramide 10 mg PO/IM/IV TDS
Promethazine 25 mg PO Nocte
Domperidone 30–60 mg PR BD or 10 mg PO QDS
Stemetil 5 mg PO TDS or 12.5 mg IM/IV
TDS; 5 mg TDS PR or 25 mg OD PR

Thromboprophylaxis

Anti-embolic stockings
Low molecular weight heparin eg: Enoxaparin 40 mg OD (<90 kg) or 60 mg OD (>90 kg)

Table 2

cases. Inpatients should be given anti-embolic stockings, low molecular weight heparin and serum electrolytes should be checked daily. Refractory cases not responding to conventional anti-emetics should prompt further investigation for another cause and a trial of corticosteroids should be considered. Biochemical thyrotoxicosis does not require treatment unless there are clinical signs of hyperthyroidism and TSH receptor antibodies are present.

Gastric reflux

A common condition affecting two-thirds of pregnant women especially in the 3rd trimester. It is exacerbated by changes in pregnancy including pressure from the enlarging uterus, increased gastric transit time, and reduced lower oesophageal sphincter pressure. These lead to reflux of gastric contents into the lower oesophagus and inflammation of the mucosa. Features include retrosternal and epigastric pain, and dyspepsia. The differential diagnosis includes peptic ulcer disease. Management includes non-pharmacological (such as sleeping semi-recumbent and avoiding food and fluids immediately before bed) and pharmacological measures. Drugs that are safe to use in pregnancy are antacids (aluminium salts cause constipation and magnesium diarrhoea); Gaviscon; metoclopramide; sucralfate; H2 receptor blockers (ranitidine safe but avoid cimetidine as effect on androgen receptors); and proton-pump inhibitors. Avoid misoprostol as it is an abortifacient, and it is also associated with congenital abnormalities, fetal death, and uterine perforation.

Peptic ulcer disease

Peptic ulcer disease is uncommon in pregnancy and this may in part be due to a protective effective of oestrogens and prostaglandins on the gastric mucosa. It usually presents with epigastric pain. Complications such as haemorrhage and perforation are rare in pregnancy but significant symptoms such as haematemesis should be investigated with upper GI endoscopy which can be safely performed in pregnancy. Pharmacological treatment includes H2 receptor blockers eg: ranitidine or proton-pump inhibitors eg: omeprazole. Misoprostol is avoided, and *Helicobacter pylori* eradication can usually be delayed until after pregnancy.

Constipation

This is another common condition in pregnancy affecting 40% of women, as physiological changes lead to decreased colonic motility and pressure of the gravid uterus on rectosigmoid colon. Risk factors include dehydration, poor dietary intake, opiate analgesia, and iron supplements.

Non-pharmacological measures such as increased fluid intake and dietary fibre are usually sufficient, with temporary cessation of oral iron. Laxatives may be required if these other measures fail, and both osmotic (lactulose, magnesium hydrochloride) and stimulant (senna, glycerol suppositories) types are safe.

Disorders of the liver and biliary tract

There are several disorders of the liver which are specific to pregnancy which are important to recognize as they are associated with significant morbidity and mortality for the mother and her fetus and delivery is the only cure. Some pre-existing conditions may only become clinically evident during pregnancy and others such as Hepatitis E have a predilection for pregnant women in whom the prognosis is significantly worse.

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