Hyperemesis, gastrointestinal and liver disorders in pregnancy

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Abstract

Pregnant women may be affected by diseases of the gastrointestinal tract or liver. These disorders can be related or unrelated to pregnancy. Conditions unrelated to pregnancy can be pre-existing or co-incident. These diseases have varying effects on obstetric outcome. Severe liver disease in pregnancy is rare. We present some common gastrointestinal and liver disorders focussing on the diagnosis, management and effects on pregnancy outcomes.

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

Overview

There are a number of normal physiological and biochemical changes associated with the liver and gastrointestinal tract in pregnancy.

Liver – pregnancy is associated with an increase in liver metabolism. Blood changes include a raised alkaline phosphatase due to placental production, albumin is reduced (although some of this is dilution due to increased blood volume in pregnancy), fibrinogen is increased. Other liver enzymes are within normal prepregnancy ranges.

Gastrointestinal – relaxation of smooth muscle in pregnancy results in decreased gut motility and consequent increased bowel transit times and constipation. There is also relaxation of the gastro-oesophageal sphincter which can result in gastric reflux, nausea and vomiting.

Pregnancy related gastrointestinal diseases

Hyperemesis

Nausea and vomiting affects up to 50% of pregnancies, however, hyperemesis only affects 0.5–1% of pregnancies. Hyperemesis is defined as severe protracted nausea and vomiting, which results in dehydration, ketosis and weight loss. It commonly starts between 6 and 12 weeks gestation and corresponds with the human chorionic gonadotrophin (HCG) rise. HCG shares a common subunit with thyroid stimulating hormone (TSH), thus causing an increase in levels of thyroxine and a drop in TSH (i.e. a biochemical hyperthyroidism). It has been suggested that this may be causative for the nausea and vomiting. Severe vomiting occurring for the first time after 12 weeks should have other potential causes investigated (such as urinary tract infection, Addison's disease, pancreatitis).

Investigations: initial investigations are listed in Table 1. Fifty per cent of cases will have abnormal LFTs (rise in transaminases and bilirubin-although no clinical jaundice) and 66% a rise in TFTs. Both should resolve with treatment. If there are concerns about true thyrotoxicosis, a history of symptoms pre-pregnancy, presence of thyroid stimulating antibodies and presence of thyroid eye disease, make this a more likely diagnosis.

Hyperemesis conveys a number of risks to the mother and fetus (Table 2).

Management: this revolves around intravenous fluid resuscitation and electrolyte balance. Care must be taken to not correct hyponatraemia too quickly as this will precipitate central pontine myelinolysis (consequently 0.9% normal saline is recommended and not double strength normal saline). It is also best to avoid dextrose containing fluids initially as these may precipitate Wernicke's encephalopathy.

Vitamin B1 (thiamine) should be supplemented to prevent Wernicke's encephalopathy. Thrombosis prophylaxis also needs to be instituted. Regular antiemetics, such as dopamine antagonists (metoclopramide), Phenothiazines (prochlorperazine), antihistamines (cyclizine) or selective 5HT3 antagonist (ondansetron) should be charted. If dyspeptic symptoms are an issue, the use of histamine receptor blockers (ranitidine) or protein pump inhibitors (omeprazole) is warranted.

Refractory cases may respond to corticosteroids. If malnutrition is an issue then use of enteral feeding or total parental nutrition may also be required. Dietician involvement should be sought early.

The normal course of hyperemesis is improvement with gestation, with the majority having resolved by midgestation. Due to the nature of hyperemesis presenting in the first trimester it is also important to ensure usual antenatal cares and early education is given. (For example, ensuring appropriate folic acid supplementation and access to chromosomal screening tests.)

Obstetric cholestasis

Obstetric cholestasis can affect 0.5–2% of pregnancies. It presents normally in the third trimester with severe pruritus (particularly of the palms and soles of feet), without a rash and with deranged LFTs and bile acids. There appears to be a genetic element with 35% of affected women having a positive family history. The causative effect appears to be an increased sensitivity to the cholestatic effect of the raised levels of oestrogen in pregnancy (progesterone may also play a role).

Investigations (Table 3)**:** these rest around exclusion of other causes of abnormal LFTs and pruritus, as obstetric cholestasis is a diagnosis of exclusion.

In 90% of cases of obstetric cholestasis there are raised liver transaminases and abnormal bile acids. However, symptoms

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Initial investigations in hyperemesis

Bloods	Full blood count
	Urea and electrolytes
	Liver function tests (LFTs)
	Thyroid function tests (TFTs)
Urine	Urinalysis for ketones
	Microscopy and culture
Radiology	Early pregnancy ultrasound scan

Table 1

may predate biochemical changes so bloods should be repeated weekly if symptoms persist.

Risks associated with obstetric cholestasis are listed in Table 4.

Whilst there are significant fetal risks, they do not correspond with severity of maternal symptoms or biochemical derangement. No surveillance method has been able to predict fetal compromise or improve outcome.

Management: this should include weekly maternal bloods for LFTs and bile acids. Prothrombin time should be checked prior to delivery if LFTs are severely deranged. Symptoms of pruritus should be managed, this can be with antihistamines or ursodeoxycholic acid (UDCA). Whilst UDCA has been shown to improve LFTs, it has not improved fetal outcomes. Dexamethasone should be used with caution and discussed with the woman due to the risk for adverse neonatal neurological outcomes.

Vitamin K deficiency is present in obstetric cholestasis due to reduced absorption likely secondary to steatorrhoea. Use of water soluble vitamin K should be considered if the prothrombin time is prolonged. This needs to be discussed carefully with the woman as early studies showed increased risk of neonatal hyperbilirubinaemia, haemolytic anaemia and kernicterus. However, at low dose such as 10 mg these risks are low; benefits include reduced risk of maternal postpartum haemorrhage and neonatal intracranial haemorrhage. Vitamin K should be offered to the newborn as routine.

Careful discussion is required around timing of delivery. As detailed above, fetal surveillance has not altered outcomes or

Hyperemesis risks

Maternal	Fetal
Wernicke's encephalopathy	40% fetal death associated with Wernicke's encephalopathy
Hyponatraemia and pontine demyelination	
Mallory–Weis tear	
Malnutrition	If >5 kg maternal weight loss or significantly reduced weight gain-lower birth weight
Psychological problems	
Thrombosis	

Table 2

Investigations for abnormal LFTs

Blood tests	FBC
	LFTs
	Coagulation profile (prothrombin time)
	Bile acids
	Urea, electrolytes and creatinine
	Glucose
	Serology for hepatitis A, B, C, E
	Serology for viral infections
	Anti-smooth muscle antibodies
	Anti-mitochondrial antibodies
Urine	Urinalysis and culture
Radiology	Liver ultrasound scan

Table 3

helped predict stillbirth. Induction may be offered from 37 weeks gestation; the mother must be aware that this may result in increased maternal morbidity and increased neonatal morbidity in the form of prematurity. There is some evidence that early induction at this time may be most appropriate in those with more severe abnormalities in liver function tests. During labour continuous monitor should be utilized.

Postnatally, liver function tests should be checked at 10 days and followed until normal. Due to obstetric cholestasis-associated sensitivity to oestrogen, contraceptives containing oestrogen should be avoided. There is a risk or recurrence in subsequent pregnancies of 90%.

Acute fatty liver of pregnancy (AFLP)

The incidence of AFLP ranges between 1 in 7000 and 1 in 12,000 pregnancies. It most commonly presents in the third trimester. Risk factors for its development include primiparity, obesity, pre-eclampsia, a male fetus and multiple pregnancy. It is thought to be associated with heterogenicity for long-chain 3-hydroxy-acyl-coenzyme A dehydrogenase (LCHAD) deficiency which is a disorder of mitochondrial fatty acid oxidation. AFLP can occur in women with this disorder if the fetus is homozygous for − fatty acid oxidation disorders.

Diagnosis is difficult as symptoms may be vague or be mistaken for pre-eclampsia or HELLP syndrome. Presentation may include pruritus, headache, nausea and vomiting, epigastric or right upper quadrant pain, diabetes insipidous with polyuria. Severe vomiting and upper abdominal pain tend to be the hallmarks of presentation and should alert the clinician to this possible diagnosis.

Obstetric cholestasis risks

Maternal	Fetal
Vitamin K deficiency	Meconium liquor and aspiration
Postpartum haemorrhage	Prematurity
	Intrauterine death

Table 4