VOMITING IN PREGNANCY

Done by :
Abd alfattah asaad - Mohammad shkanbeh
Sabaa albrezat – yaqeen malahmeh
Shorouq almaaith

Gastrointestinal changes during pregnancy

A number of changes happen in the gastrointestinal system normally during pregnancy, and these changes may in part be responsible for the common symptoms of nausea and vomiting during pregnancy, which are:

- Decreased lower esophageal pressure
- Decreased gastric peristalsis and delayed gastric emptying
- Gastrointestinal motility is inhibited, with increased small and large bowel transit times

PATHOPHYSIOLOGY OF N&V IN PREGNANCY

The cause of nausea and vomiting of pregnancy is unknown, but may relate to the change in
.hormonal level
An increase in the circulating level of the hormone estrogen.
Related to increased estrogen levels,
a similar form of nausea is also seen in some women who use hormonal contraception or hormone
replacement therapy.
An increase in progesterone. It is responsible for the gastrointestinal changes during pregnancy.
An increase in HCG. It is probably not the HCG itself that causes the nausea. More likely, it is the
HCG stimulating the maternal ovaries to secrete estrogen and progesterone, which in turn causes
the nausea.

DDX

Differential diagnosis	Important clinical features	Investigations
Physiological (nausea and vomiting of pregnancy [NVP])	Associated nausea 'Morning sickness' is a misnomer; nausea and vomiting may occur throughout the day Onset before 12 weeks' gestation, commonly 6–7 weeks Usually remits by 12–16 weeks' gestation	
Hyperemesis gravidarum	Onset before 12 weeks' gestation. Nausea and vomiting are severe enough to cause marked weight loss, dehydration and ketonuria. May be associated with abnormal thyroid and liver function. More common with multiple and molar pregnancy. Usually recurs in each pregnancy	Urea + electrolytes Liver function tests Thyroid function tests Mid-stream urine
Drug-induced, e.g., iron supplements, antibiotics, ergometrine		
Infection, e.g., urinary tract infection, gastroenteritis, cholecystitis	See 'Abdominal pain', Table 16.17	Mid-stream urine Stool culture Blood cultures Venous lactate Liver and renal US
Pre-eclampsia/HELLP/AFLP	See 'Abdominal pain', Table 16.17	
Metabolic causes, e.g., uraemia, hyperglycaemia, hypercalcaemia, Addison's disease		Urea + electrolytes Blood glucose Liver function tests and calcium

Morning sickness

Morning sickness is the mild nausea, that may or may not be associated with vomiting which commonly happens during pregnancy.

It occurs in about 70-80% of all pregnancies. It typically starts early (~6 weeks).

Although the symptoms are often most pronounced in the first trimester, they are by no means confined to it.

Despite common usage of the term ‘morning sickness’, in only a minority of cases are the symptoms solely confined to the morning.

Nausea and vomiting in pregnancy tends to be mild and self-limited and is not associated with adverse pregnancy outcome.

Hyperemesis gravidarum

Severe or protracted vomiting in early pregnancy, sufficient to cause fluid, electrolyte and nutritional disturbances.

Hyperemesis gravidarum (HG) occurs in 0.3%–3% of pregnancies

Clinical features of HG

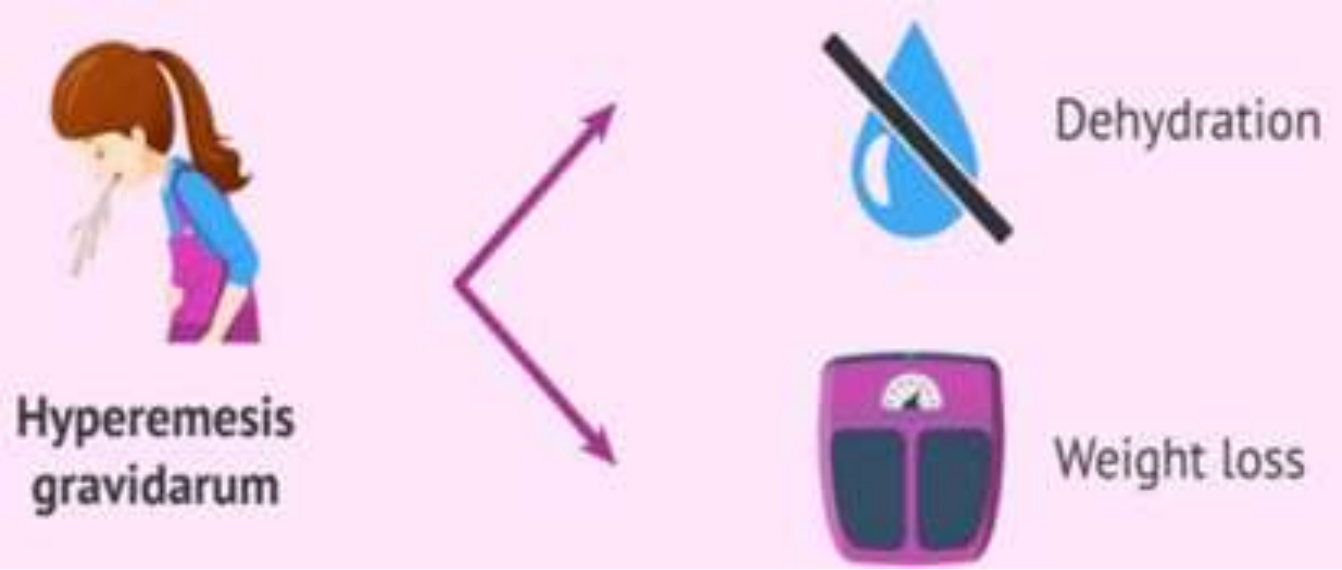
Onset is always in the first trimester, usually weeks 6-8

Severe protracted nausea and vomiting

Weight loss of more than 5% of pre-pregnancy weight Dehydration and electrolyte imbalance, including ketosis

There are usually signs of dehydration with postural hypotension and tachycardia and there may be muscle wasting.

There may be associated ptyalism (excessive salivation) and associated spitting



Etiology of hyperemesis gravidarum

The exact pathophysiology behind HG is poorly understood, however, various hormonal, mechanical and psychological factors have been implicated.

The physiological gastrointestinal changes during pregnancy may well exacerbate the symptoms of hyperemesis gravidarum, but are unlikely to be causative in isolation.

There is a direct relationship between the severity of HG and the degree of bio-chemical hyperthyroidism, and it has been suggested that the raised thyroxine levels or suppressed TSH may be causative.

Hyperthyroidism and HG

The level of human chorionic gonadotropin (hCG), which shares a common α-subunit with TSH, is directly correlated with the severity of vomiting and free thyroxine concentrations and inversely correlated with TSH levels.

hCG probably acts as a thyroid stimulator in patients with HG. There is structural homology not only in the hCG and TSH molecules but also in their receptors, and this suggests the basis for the reactivity of hCG with the TSH receptor.

The positive correlation between severity of HG and hCG levels explains the increased incidence of this condition in multiple pregnancy and hydatidiform mole.

The picture is that of a biochemical hyperthyroidism with a raised free thyroxine and/or a suppressed thyroid-stimulating hormone (TSH).

Patients with these abnormalities are clinically euthyroid without thyroid anti-bodies, except in the very rare case of thyrotoxicosis presenting in early pregnancy.

The abnormal thyroid function tests do not require treatment with anti-thyroid drugs and resolve as the hyperemesis improves.

There is an increased incidence of gestational thyrotoxicosis demonstrated in Asians compared to Europeans.

Investigations:

Blood tests typically reveal the following:

Hyponatremia Hypokalemia

Hypochloremic metabolic alkalosis Low serum urea

Ketonuria

Raised hematocrit level and increased specific gravity of the urine Liver function tests → abnormal in 50% of cases

Thyroid function tests → abnormal in ~66% of cases.

An ultrasound (US) scan of the uterus could be done to rule out multiple gestation or hydatidiform mole.

Risk factors:

primigravid

-multiple gestation

-molar pregnancy

-heartburn

-female fetus (1.27)

-non drinkers,non smokers

-family history or previous HG

Diagnosis and Assessment Tri

>5% pregnancy weight loss

dehydration

electrolyte imbalance

Lab studies

-Liver enzymes and bilirubin

-Blood glucose,, Amylase/lipase

-TSH, Free thyroxine

-Full blood count, Serum Electrolyte and ketones

Urine culture , Urinanalysis for ketones and specific gravity

Choose the answer that describe the best your situation in the worst day of NVP in their current pregnancy, which could have occurred recently or several weeks before the questionnaire.

Questions \ Score	1	2	3	4	5
Question 1. For how long have you felt nauseated or sick to your stomach?	Not at all	< 1 hour	1 to 3 hours	3 to 6 hours	> 6 hours
Question 2. How many times do you vomit or throw up?	Never	1 to 2	3 to 4	5 to 6	≥ 7
Question 3. How many times have you had retching or dry heaves without bringing anything up?	Never	1 to 2	3 to 4	5 to 6	≥ 7

PUQE total score; mild if the score was between 3–6 points, moderate if 7–12 points, severe if 13 points or higher.

Calcium, hematocrit, hepatitis panel…-ECG

-Imaging : Obstetric ultrasonography.

Effect of HG on pregnancy:

Maternal complications

.The main risks to women with hyperemesis gravidarum are dehydration and electrolyte imbalances

Women with prolonged hyperemesis gravidarum are at greater risk for preterm labor and preeclampsia according to the HER Foundation

*Vitamins deficiency ::

Vitamin B1 (thiamine) : Wernicke’s encephalopathy due to vitamin B1 (thiamine) deficiency is a fatal but reversible medical emergency

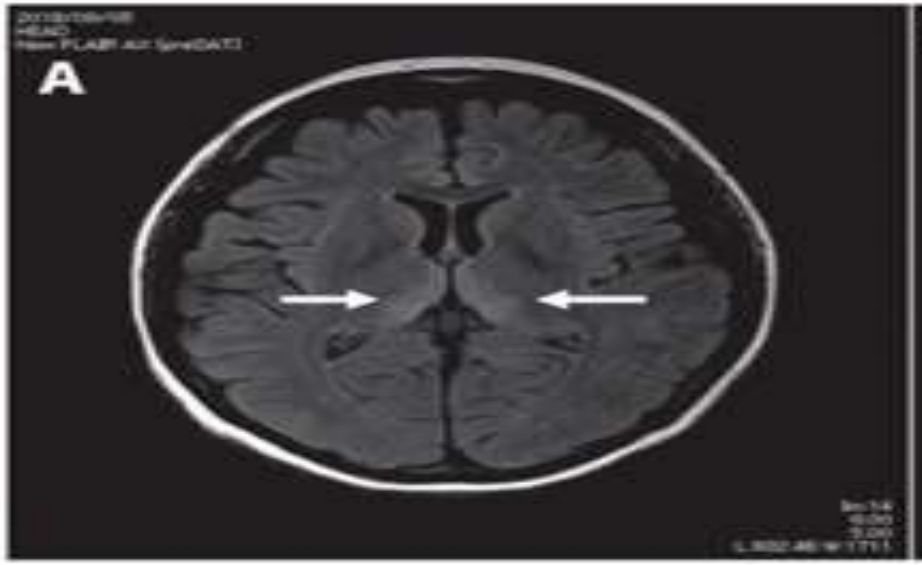
-Diagnosis of Wernicke’s encephalopathy is clinical and can be rapidly confirmed with (MRI) Others : cyanocobalamin (vitamin B12) and pyridoxine (vitamin B6)

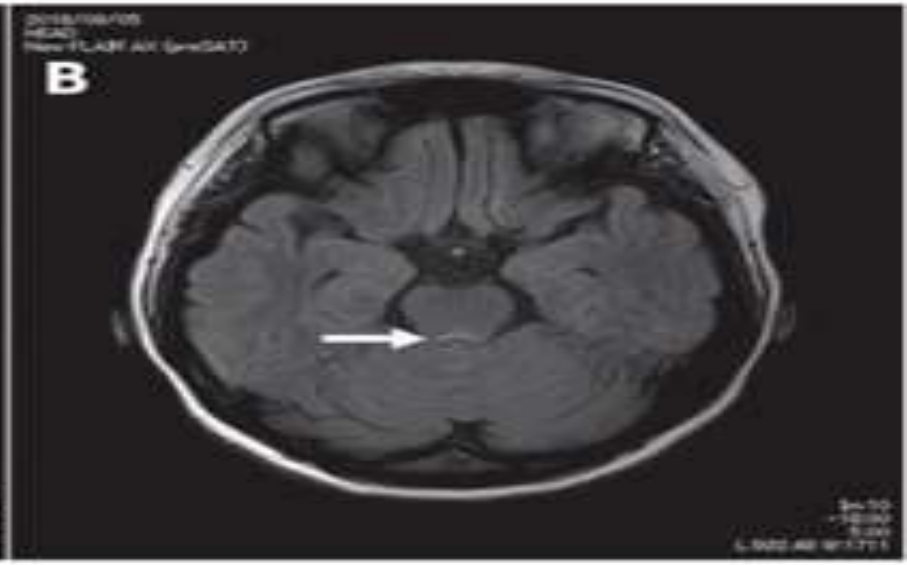
causing anaemia and peripheral neuropathy.

thiamine deficiency
↓
brain tissue ischaemia + cell death
↓
WERNICKE'S → 1. Acute confusional state 2. Ophthalmoplegia 3. ataxia
↓
KORSAKOFF'S → 1. Amnesia 2. Confabulation 3. Psychosis

Wernicke Syndrome

1. **Encephalopathy**
   - Disorientation
   - Indifference
   - Inattentiveness
2. **Ocular motor dysfunction**
   - Nystagmus
   - Lateral rectus palsy
   - Conjugate gaze palsies
3. **Ataxia**
   - Gait
   - Stance





Hyponatraemia

(plasma sodium <120 mmol/L) may cause lethargy, seizures and respiratory arrest

Correct the sodium to reach normal rang (135-145 mmol/L) By add 6mmol per day Or 3 mmol per hr

Osmotic demyelination syndrome may associate with Locked in syndrome

Both severe hyponatraemia and, particularly, its rapid reversal may precipitate central pontine myelinolysis (osmotic demyelination syndrome). This is associated with symmetrical destruction of myelin at the centre of the basal pons and causes pyramidal tract signs, spastic quadraparesis, pseudobulbar palsy and impaired consciousness.

Central pontine myelinolysis and Wernicke's encephalopathy may co-exist with HG, and thiamine deficiency may render the myelin sheaths of the central pons more sensitive to changes in serum sodium.

other complications

*Mallory–Weiss tears Esophageal tears

*Stress ulcer in stomach

*Venous thromboembolism *Jaundice, Renal problem, V k deficiency.

Fetal complication:

Wernicke's encephalopathy is associated with a 40% incidence of fetal death.

Infants of mothers with severe HG (associated with abnormal biochemistry weight

loss >5% and recurrent admission) have significantly lower birth weights and birth- weight percentiles compared to infants of mothers with mild HG and those of the general antenatal population

Management of hyperemesis gravidarum.

The potential maternal and fetal complications of HG argue for early and aggressive treatment. All patients with HG require emotional support with frequent reassurance and encouragement from nursing and medical staff.

Drugs that may cause nausea and vomiting should be temporarily discontinued. The commonest

example is iron supplements.

Any woman who is ketotic and unable to maintain adequate hydration requires i.v.fluids and parenteral anti-emeticscases

For less severe, outpatient management with administration of i.v.fluid therapy and anti-emetics as required should be first line

The natural history of HG is gradual improvement with increasing gestation, although in a minority of women symptoms may persist beyond 20 weeks' gestation.The only definitive cure is termination of the pregnancy.

Suggested management algorithm for nausea and vomiting in pregnancy and HG

Mild nausea and vomiting Urinary ketones negative	Moderate dehydration Urine ketones 1–2+	Severe dehydration Urine ketones 3–4+
Community-based care	Outpatient-based care	Inpatient admission
Encourage oral fluids and small frequent meals	i.v. fluids (1 L normal saline + 20 mmol K over 2 hours × 2) Thiamine supplements	i.v. fluids (1 L normal saline + 40 mmol K, 3 L/day) i.v. thiamine
Oral anti-emetics	i.v. anti-emetics e.g., Cyclizine 50 mg	Regular i.v. anti-emetics Prophylactic LMWH

Intravenous fluid therapy

-Adequate and appropriate fluid and electrolyte replacement is the most important component of management.

-Infusion of dextrose-containing fluids (dextrose saline, 5% dextrose, 10% dextrose) is mistakenly thought by some to be desirable to provide the patient with calories, but this assumption is. erroneous and dangerous

-Normal saline (sodium chloride 0.9%; 150 mmol/L Na+) and Hartmann's solution (sodium chloride 0.6%; 131 mmol/L Na+) are appropriate solutions.

Correction of the hypokalaemia is essential and it is usually necessary to use infusion bags containing 40 mmol/L of potassium chloride.

There is no place for the use of double-strength saline (2n saline), even in cases of severe hyponatraemia, as this results in too rapid a correction of serum sodium with the risk of central pontine myelinolysis. (so hypertonic saline is CI)

Fluid and electrolyte regimes must be adapted daily and titrated against daily measurements of serum sodium and potassium and fluid balance

Thromboprophylaxis

HG is a risk factor for venous thrombosis probably because of dehydration and immobilization

.Therefore, all women admitted with hyperemesis should receive appropriate doses

of low-molecular-weight heparin (LMWH)

Thiamine therapy

• Thiamine supplementation should be given to anyone suffering from prolonged vomiting.Requirements for thiamine increase during pregnancy to 1.5 mg/day, and women

admitted with a diagnosis of hyperemesis have usually been vomiting for at least 1–2 weeks prior to admission.

• If the woman is able to tolerate tablets, thiamine can be given as thiamine hydrochloride tablets

25–50 mg thrice daily. If i.v.treatment is required for those unable to tolerate tablets, this is given as thiamine 100 mg diluted in 100 mL of normal saline and infused over 30–60 minutes.

Alternatively, this may be given as Pabrinex®, which contains 250 mg of thiamine hydrochloride per pair of ampoules.The i.v.preparation is only required weekly.

• Treatment (as opposed to prevention) of Wernicke’s encephalopathy requires much higher doses of thiamine.

Pharmacological therapy---Anti-emetics

Women presenting to secondary care who do not respond to i.v.fluids and electrolytes aloneshould be offered anti-emetic therapy.

Extensive data exist to show a lack of teratogenesis or other adverse pregnancy outcomes with

-Antihistamines (H1-receptor antagonists, e.g., promethazine, cyclizine, cinnarizine, doxylamine, dimenhydrinate)

-Phenothiazines (chlorpromazine, prochlorperazine)

-Dopamine antagonists (metoclopramide, domperidone)

-Serotonin (5HT3) inhibitors (ondansetron)

If symptoms do not improve, the anti-emetic should be prescribed and given regularly

First line therapy

Cyclizine	50 mg p.o., i.m. or i.v. 8 hourly
Prochlorperazine	5–10 mg p.o., i.m., i.v. or p.r. 6–8 hourly 12.5 mg i.m./ i.v. 8 hourly 25 mg p.r. daily
Promethazine	12.5–25 mg i.m., i.m., i.v. or p.r. 4–8 hourly
Chlorpromazine	10–25 mg i.m., i.v. or i.m. 4–6 hourly 50–100 mg p.r. 6–8 hourly
Doxylamine plus pyridoxine	10 mg of each up to 8 tablets per day

Second line therapy

Metoclopramide	5–10 mg i.m., i.v. or i.m. 8 hourly (maximum 5 days duration)
Domperidone	10 mg i.m. 8 hourly 30–60 mg p.r. 8 hourly
Ondansetron	4–8 mg i.m. 6–8 hourly 8 mg over 15 minutes i.v. 12 hourly

Side effects

include drowsiness, particularly with the phenothiazines, and extrapyramidal effects

and oculogyric crises, particularly with metoclopramide. Extrapyramidal effects usually abate after discontinuation of the drug and oculogyric crises may be treated with antimuscarinic drugs such as

benzatropine 1–2 mg intramuscularly (i.m.) or i.v.

Metoclopramide is safe and effective but because of the risk of extrapyramidal side effects, it should be used for second-line therapy.

Ondansetron is safe and effective, but because data are more limited it should be used as second-line therapy

Histamine2 (H2)-receptor blockers and proton pump inhibitors

.

H2-receptor blockers (e.g., ranitidine) and the PPIs (e.g., omeprazole) are used in cases where oesophagitis or gastritis accompanies the nausea and vomiting of HG.They are safe for use in pregnancy.

Corticosteroids

-Corticosteroids have resulted in dramatic and rapid improvement in case series of women with

severe refractory HG.,Randomized studies also support a beneficial effect for those with very severe disease.

-They should not be used until conventional treatment with i.v.fluid replacement and regular parenteral anti-emetics has failed

-They should not be used for those with recurrent admissions who respond to parenteral anti-emetic therapy.

-Suggested doses are prednisolone 40–50 mg orally (p.o.) daily in divided doses or hydrocortisone100 mg i.v.twice daily.

-In cases who do respond to steroid therapy, the dose must be reduced slowly and prednisolone

cannot usually be discontinued until the gestation at which the HG would have resolved spontaneously (in some extreme cases this occurs at delivery).

-In cases who do not respond to steroid therapy, it should be discontinued.

Enteral feeding

If women fail to respond to i.v.fluid and anti-emetic treatment and corticosteroid treatment, then nutritional support may be required in the form of enteral or parenteral feeding.

-When the gastrointestinal tract is intact and usable, it is preferable to use enteral rather than parenteral hyperalimentation to treat malnutrition.

-Enteral feeding options include nasogastric (NG), nasoduodenal or NG tubes, or percutaneous endoscopic gastrostomy or jejunostomy feeding.

Total parenteral nutrition

-TPN with peripherally inserted central catheters (PICC line) is often better tolerated than enteral,but it carries more risk.

-TPN has also been shown to have a rapid therapeutic effect in some cases

-Metabolic and infectious complications are a risk and strict protocols and careful monitoring are obligatory.The central line site must be inspected regularly for signs of infection.

-Phlebitis and thrombosis are other recognized complications of TPN.

-Because TPN involves the use of high concentrations of glucose, thiamine supplementation is mandatory.

-Parenteral feeding is usually reserved for extremely severe life-

Pre-pregnancy counselling/recurrence

Hyperemesis almost invariably recurs in subsequent pregnancies.

In very severe cases, especially those necessitating TPN or termination of the pregnancy, women may be advised that studies suggest a beneficial effect of steroids, which may provide a therapeutic option in subsequent pregnancies.Prompt institution of anti-emetic therapy is important in subsequent pregnancies.

Hyperemesis gravidarum—points to remember

- HG is a diagnosis of exclusion.
- HG may be associated with both abnormal liver and thyroid function tests.
- Adequate and appropriate (normal saline and potassium chloride) fluid and electrolyte replacement is the most important component of management.
- Thiamine supplementation to prevent Wernicke's encephalopathy and thromboprophylaxis should be given to all women admitted with hyperemesis.
- The common anti-emetics are not teratogenic.
- Corticosteroids may have a role to play in severe resistant cases.

THANK YOU