Nausea and Vomiting in Pregnancy (NVP) and Hyperemesis Gravidarum (HG) Guideline

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Contents

1. Introduction 3

2. Diagnosis 3

3. Clinical assessment and baseline investigations 4

4. Management 5

5. Multi-Disciplinary Team approach 8

6. References 8

1. Introduction

NVP affects up to 90% of pregnant women and HG occurs in around 0.3-3.6%. It usually begins between 4 and 7 weeks gestation, peaks between 9-16 weeks and resolves 16-20 weeks gestation. It is thought to be related to hypersensitivity to the growth differentiation factor-15 (GDF15). GDF15 is made when genes in the placenta are activated, and variations in the gene can be identified in individuals with HG. Onset after 16 weeks gestation usually suggests an alternative cause for symptoms.

Definitions:

NVP is the symptom of nausea and/or vomiting during early pregnancy (<16 weeks gestation) where there are no other causes identified.

HG is the severe form of NVP which is severe enough to cause an inability to eat and drink normally and strongly limits daily activities of living. Often there is more than 5% weight loss, malnutrition, dehydration and electrolyte imbalance.

Risk factors:

Increased placental mass (multiple pregnancy, molar pregnancy), first pregnancy, and previous history of HG. Ethnic minorities, and women with type 1 diabetes are also at higher risk.

Consequences:

Maternal complications include weight loss, acute kidney injury, electrolyte imbalance (hyponatraemia, hypokalaemia), gastro-reflux disease, and venous thromboembolism. In severe cases metabolic acidosis may occur. It can often lead to a deterioration in mental health.

Fetal complications include preterm birth, and small for gestational age.

2. Diagnosis

NVP should only be diagnosed when onset is in the first trimester of pregnancy and other causes of nausea and vomiting have been excluded.

Differential diagnoses to consider, based on the history/examination/investigations:

1) Infection +/- sepsis: Common sources include urinary tract infection, pneumonia, gastroenteritis, cholecystitis. While NVP and HG can have overlapping signs (e.g. low BP, raised HR), signs such as high/low temperature or high respiratory rate, as well as other symptoms in addition to the N&V (such as diarrhoea, cough, abdominal pain, dysuria/urinary frequency/haematuria, back pain, rashes) should prompt consideration of other diagnoses.

2) Peptic ulcer disease: It is important to establish any previous history of PUD including previous treatment for H-Pylori. Check whether the patient was previously taking a PPI (Proton Pump Inhibitor) which they may have stopped after becoming pregnant. Establish any other symptoms; heartburn, epigastric pain, acid reflux, belching.

3) Pancreatitis: Again, previous episodes are important to enquire about. Establish if there are any risk factors e.g. alcohol excess or known gallstones. Pancreatitis usually causes severe abdominal pain, and there may be additional symptoms e.g. dark urine, pale stools or jaundice if the cause is gallstones.

4) Hepatitis: There are multiple aetiologies of hepatitis including infective and non-infective causes. Liver disease can have a very varied presentation, but RUQ pain, jaundice and malaise are common. Key points from the history should include recent travel, any unwell close contacts and any history of intravenous drug use.

5) Metabolic conditions: The symptoms of diabetic ketoacidosis can overlap with NVP/HG; establish any history of diabetes and do a BM. Thyroid disease can present with N&V; other symptoms/signs such as goitre may be present. Other metabolic causes such hyperparathyroidism/hypercalcaemia and Addison's disease should also be considered if there are associated symptoms/signs.

6) Neurological conditions: Consider if there are additional symptoms and signs e.g. headache, visual changes, limb or facial weakness, vertigo, tinnitus, hearing loss, neck stiffness. Causes include migraine, meningitis, stroke, severe hypertension, labyrinthitis, Ménière's disease.

7) Drug induced: A thorough drug history including over the counter medications and recreational use is essential.

3. Clinical assessment and baseline investigations

History:

- NVP/HG in previous pregnancies and identify any risk factors
- Symptoms in addition to nausea and vomiting; fevers, rigors, rash, abdominal or back pain, urinary symptoms, diarrhoea, vaginal discharge or bleeding, heartburn/reflux, jaundice, neurological symptoms. Please see the differential diagnosis section in section 2 for further details
- Psychological impact and mental well being
- Drug history e.g. iron tablets, antibiotics, over the counter medications, recreational drugs. Any anti-emetics already tried is important
- The Pregnancy-Unique Quantification of Emesis (PUQE) index below should be used to establish the severity of NVP.

PUQE 24 score

In the last 24 hours, for how long have you felt nauseated or sick to your stomach?	Not at all (1)	1 hour or less (2)	2-3 hours (3)	4-6 hours (4)	More than 6 hours (5)	/5

In the last 24 hours have you vomited or thrown up?	Not at all (1)	1-2 times (2)	3-4 times (3)	5-6 times (4)	7 or more times (5)	/5
In the last 24 hours, how many times have you had retching or dry heaves?	None 91)	1-2 times (2)	3-4 times (3)	5-6 times (4)	7 or more times (5)	/5
Total score (mild ≤ 6, moderate 7-12, severe 13-15)						/15

Examination:

- Temperature, respiratory rate, heart rate, oxygen saturations, blood pressure
- Maternal Weight
- Fluid status – assess the mucous membranes and skin for evidence of dehydration
- Abdominal examination – significant tenderness could suggest other diagnoses
- Neurological signs such as confusion, nystagmus or ataxia (which could indicate Wernicke's encephalopathy)

Investigations:

- Urine dipstick and MSU if indicated. Note ketonuria is not an indicator of dehydration and should not be used to assess severity.
- Urea and electrolytes (U&E), full blood count (FBC), blood glucose (BM). Consider amylase if clinical suspicion of pancreatitis. In severe cases consider a VBG to exclude metabolic disturbances
- In treatment resistant cases or if there has been a previous admission: thyroid function tests (TFTs), liver function tests (LFTs), amylase, bone profile. Two thirds of women with HG have abnormal TFTs but rarely have thyroid antibodies and are euthyroid clinically. The abnormal TFTs (raised T4 and low TSH) therefore do not need treatment if the woman is responding to NVP / HG treatment.
- If the patient has not yet had an ultrasound scan (USS) this should be organised (to confirm viability and exclude multiple pregnancy)

4. Management

Women with mild NVP should be cared for in the community with antiemetics
PUQE-24 scores of 3-12 with no complications (dehydration, electrolyte imbalance, weight loss >5%): community management is appropriate. Anti-emetics should be prescribed and the patient provided with written information (Dietary information leaflet, Nausea and Vomiting in Pregnancy Patient Information leaflet) and directed to support groups such as Pregnancy Sickness Support.

Avoid iron-containing preparations as these may exacerbate symptoms. If iron is required, consider alternative routes of administration.

Ambulatory day care should be used when community measures have failed.

- PUQE score of ≥13 with no complications and not refractory to anti-emetics: ambulatory day assessment management until clinical improvement (patient can return following day for further IVI if required) .
- Intravenous fluids
- Thiamine supplementation. Thiamine stores can deplete rapidly and cause tachycardia, weakness and decreased deep tendon reflexes.

Inpatient care for women who have continued NVP despite antiemetics, or comorbidity

- Any PUQE score with complications e.g. inability to tolerate oral anti-emetics, co-morbidity, or unsuccessful ambulatory day assessment management: in-patient management
- If not tolerating oral anti-emetics parenteral medication may be more effective.
- Electrolyte results should be used to help guide fluid management.
- Antiemetics should be used in combination.
- Corticosteroids should be reserved for cases where standard therapies have been ineffective and used in combination with antiemetics. Women who have corticosteroids should have screening for Gestational diabetes.
- Referral to secondary care: primary care providers should be guided by the PUQE score criteria outlined above. Refractory symptoms despite a trial of two or more different anti-emetics, clinical concern or complications (see above) should prompt consideration of discussion with or referral to secondary care.
- Where concerns arise around mental health then these should be managed as per the Maternity Perinatal Pathway. https://wisdom.nhs.wales/health-board-guidelines/swansea-bay-maternity-file/maternity-perinatal-mental-health-guideline2abmu-maternity-guideline-2022pdf/

Women with previous bariatric surgery

A previous history of gastric reduction surgery (gastric band, gastric bypass, gastric sleeve) may cause malabsorption of oral medication and increase the risk of nutrient and vitamin deficiency, especially thiamine and vitamin K. Specialist advice may be required for these women.

Prescribing:

A combination of different classes of anti-emetics should be tried in women who do not respond to a single agent.

1st Line antiemetics	**Prochlorperazine** 5-10mg tds PO, or 3-6mg bd buccal 12.5mg IM bd **Cyclizine** 50mg tds PO

	Promethazine 12.5 – 25mg tds PO or IM **Doxylamine and Pyridoxine** 20/20mg PO at night, increase to additional 10/10mg morning and lunchtime if required
2nd line antiemetics	**Metoclopramide** 5-10mg tds MAX 5 days (extrapyramidal side effects and oculogyric crisis) **Ondansetron** 4-8mg tds PO or buccal (if unable to tolerate PO) *Caution if under 12 weeks as slight increase in cleft palate risk from 11 per 10,000 to 14 per 10,000.*
3rd line antiemetics	**Corticosteroids** hydrocortisone 100mg bd IV. Once stable change to Prednisolone PO 40-50mg od then reduce by 5mg per week to lowest dose to control symptoms.
Thiamine	100mg od PO
Omeprazole	20mg od PO

Day Assessment Management on the Antenatal Day Assessment Unit (ADAU):

- Should include a VTE risk assessment +/- LMWH prescription
- Fast re-hydration with 1L of Hartmann's over 2 hours then 1L of NaCl 0.9% with 20mmol of KCl over 2 hours (Avoid dextrose containing solutions as these can precipitate Wernicke encephalopathy)
- Prescription for thiamine and anti-emetics (considering what has been tried already)
- Organisation of USS if the patient has not yet had one during this pregnancy
- If patient is clinically improved with no complications, the patient can be discharged home with anti-emetic TTO + PPI, plus the written information as listed for community management above
- Important points to note:
- The ADAU unit can usually manage 1 patient with NVP at a time. When ADAU is not available women should be admitted to gynae (<20 weeks gestation) or ward 19. Management should still follow the same process as outlined above.
- Patients requesting or awaiting a planned termination of pregnancy (TOP) can be offered management of NVP on the gynae ward.

In patient management:

- Patients should have a VTE risk assessment and be prescribed LMWH unless contraindicated until at least discharge from inpatient management.
- Daily U&Es should be monitored while receiving IV fluids
- USS should be arranged if the patient has not yet had one during this pregnancy
- Consider steroids if symptoms refractory to other anti-emetics.
- Women with severe symptoms or symptoms extending into late second trimester or beyond should be referred to ANC for serial growth scans
- Referral to Dietetics for nutritional support

Alternative therapies
Women may wish to try ginger (if mild) and/or acupuncture/acupressure. There is some evidence to support the use of acupressure and women can be reassured that neither of these are harmful in pregnancy.

5. Multi-Disciplinary Team approach

Other healthcare professionals should be involved in the care of women with severe HVP/HG, including midwives, nurses, dieticians, pharmacists, endocrinologists, gastroenterologists, mental health professionals, as appropriate.

6. References

1. *Nelson-Piercy, C., Dean, C., et al. The Management of Nausea and Vomiting in Pregnancy and Hyperemesis Gravidarum Green top guideline 69. BJOG. 2024; 131 (7): p1-30*
   https://obgyn.onlinelibrary.wiley.com/doi/10.1111/1471-0528.17739

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   https://cks.nice.org.uk/topics/nausea-vomiting-in-pregnancy/

Maternity Services

Checklist for Clinical Guidelines being Submitted for Approval

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