

# The management of nausea and vomiting during pregnancy

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## Abbreviations

- **HELP:** Hyperemesis Level Prediction tool.
- **HG:** Hyperemesis gravidarum.
- **NVP:** Nausea and vomiting during pregnancy.
- **PND:** postnatal depression, anxiety.
- **PTSD:** post-traumatic stress disorder.
- **PUQE:** Pregnancy-Unique Quantification of Emesis tool.

## Glossary

- **Nausea and vomiting in pregnancy (NVP):** NVP is defined as symptoms of nausea, vomiting and/or dry retching commencing before 16 gestational weeks without another cause.
- **Hyperemesis in pregnancy (HG):** It is persistent vomiting with weight loss not related to other causes along with an objective measure of acute starvation such as carbohydrate depletion, electrolyte abnormalities and/or acid-base disturbance.

## Executive Summary

This guideline offers evidence-based recommendations on the management of nausea and vomiting during pregnancy. The recommendations are intended to provide healthcare professionals with practical guidance on appropriate and timely diagnosis and choosing the best evidence-based treatment modality of nausea and vomiting during pregnancy resulting in improving health outcomes for people with this condition that may considerably affect fetal and maternal health.

## List of Recommendations

Recommendation	Strength
<b>Diagnosis of nausea and vomiting during pregnancy</b>	
NVP is diagnosed when onset is prior to 16 weeks of gestation and other causes of nausea and vomiting have been excluded.	Strong
HG is diagnosed when symptoms start in early pregnancy, nausea and/or vomiting are severe enough to cause an inability to eat and drink normally and strongly limits daily activities of living (see the differential diagnosis of NVP in appendix1).	Strong
An objective and validated index of nausea and vomiting such as the PUQE tool (see appendix 2) can be used to classify the severity of NVP and HG.	Conditional
Clinicians should be aware of the features in history, examination and investigation that allow appropriate assessment of NVP and HG and to monitor severity.	Strong
Ketonuria is not an indicator of dehydration in pregnancy and should not be used to assess severity.	Strong
<b>Non-Pharmacological therapies of NVP and HG</b>	
Avoid an empty stomach at all times, with small and frequent meals every 1–2h.	Strong
Prevent a full stomach (ie. not mixing solid with liquid, avoiding large meals).	Strong
Eat dry food, high-protein snacks, and crackers in the morning before arising.	Strong
Avoid strong tasting and spicy food, eliminate supplemental iron.	Strong

Ginger, has shown a beneficial effect in reducing nausea symptoms, but not in reducing vomiting.	Strong
We recommend against acupuncture, acupressure and hypnosis.	Strong
<b>Pharmacological therapies</b>	
Combinations of different drugs should be used in women who do not respond to a single antiemetic.	GPS
For women with persistent or severe HG, non-oral routes may be necessary and more effective than an oral regimen	Conditional
<p><b>Stepwise approach for mild and moderate NVP without hypovolemia:</b></p> <ul style="list-style-type: none"> <li>- Doxylamine/pyridoxine (vitamin B6) is recommended as the first-line therapy for mild-moderate NVP: Doxylamine/pyridoxine 20/20mg PO at night, increase additional 10/10 mg in morning and 10/10mg at lunchtime if required.</li> </ul> <p><b>If no adequate response, ADD antihistaminic:</b></p> <ul style="list-style-type: none"> <li>- Cyclizine 50 mg PO, IM or IV 8 hourly</li> <li>- Promethazine 12.5–25 mg 4–8 hourly PO, IM or IV.</li> </ul> <p><b>If no adequate response, ADD dopamine antagonists:</b></p> <ul style="list-style-type: none"> <li>- Prochlorperazine 5–10 mg 6–8 hourly PO (or 3 mg buccal); 12.5 mg 8 hourly IM/IV; 25 mg PR daily.</li> <li>- Metoclopramide 5–10 mg 8 hourly PO, IV/IM/SC.</li> <li>- Domperidone 10 mg 8 hourly PO; 30 mg 12 hourly PR.</li> </ul> <p><b>If no adequate response, ADD:</b></p> <ul style="list-style-type: none"> <li>- Ondansetron 4 mg 8 hourly or 8 mg 12 hourly PO; 8 mg over 15 minutes 12 hourly IV; 16 mg daily PR (Women taking ondansetron may require laxatives if constipation develops).</li> </ul> <p><b>If no adequate response, ADD:</b></p> <ul style="list-style-type: none"> <li>- Hydrocortisone 100 mg twice daily IV and once clinical improvement occurs, convert to prednisolone 40–50 mg daily PO, with the dose gradually tapered (by 5-10 mg per week) until the lowest maintenance dose that controls the symptoms is reached (Corticosteroids should be reserved for cases where standard therapies have failed; when initiated they should be prescribed in addition to previously started effective antiemetics.</li> <li>- Women taking corticosteroids should have their blood pressure monitored and a screen for diabetes mellitus).</li> </ul>	Strong
Acid-reducing agents can be used as adjunctive therapy in patients with heartburn/acid reflux and NVP.	Conditional
In women with severe NVP or HG, input could be sought from other allied professionals.	Conditional
Women with previous or current NVP or HG should consider avoiding iron-containing preparations if these exacerbate symptoms or consider alternative route of administering iron.	Conditional
Histamine type-2 receptor blockers or proton pump inhibitors may be used for women developing gastro-oesophageal reflux disease, oesophagitis or gastritis.	Conditional
<b>Management of NVP-HG with hypovolemia</b>	

Hospital admission for close monitoring and ongoing treatment is appropriate for those with persistent inability to tolerate oral intake resulting in hypovolemia requiring intravenous replacement fluid, and failure of oral and/or intravenous antiemetic therapy.	Strong
The goal of inpatient management is to restore oral intake to enable adequate hydration and nutrition and use of oral antiemetic therapy after discharge.	Strong
The decision to discharge needs to be individualized based on the patient's ability to access outpatient resources.	Strong
A baseline electrocardiogram is indicated in patients with electrolyte abnormalities requiring replacement.	Strong
<b>Fluid replacement:</b> <ul style="list-style-type: none"> <li>- Aggressively rehydrate with up to 2 liters of IV crystalloid over two hours (preferably with lactated Ringer's due to decreased incidence of acute kidney injury compared with normal or isotonic saline).</li> <li>- After initial resuscitation, titrate IV fluids to maintain urine output at least 100 mL/hour or continue at a rate of 125 to 150 mL/hour, with close monitoring of oral intake and urine output.</li> <li>- Then switch to dextrose-saline (dextrose 5% in 0.45% saline) at a rate of 150 mL/hour. For patients with normal potassium levels, add 10 mEq potassium chloride for each 500 ml.</li> </ul>	Strong
<p>Urea and serum electrolyte levels should be checked daily in women requiring intravenous fluids.</p> <p>In patients with electrolyte imbalance, consult intensive care specialist to correct the imbalance.</p>	GPS
<b>Thiamine:</b> <ul style="list-style-type: none"> <li>- To reduce the risk of Wernicke encephalopathy, 100 to 200 mg thiamine (vitamin B1) should be added to the initial fluid resuscitation and then daily thereafter while the patient is taking nothing-by-mouth or for two to three days in patients with oral intake.</li> <li>- If Wernicke encephalopathy is suspected, treat with 200 to 500 mg IV every eight hours for 2 to 7 days, followed by 250 mg once daily for an additional 3 to 5 days, followed by maintenance therapy 100 mg daily until no longer at risk for deficiency. Thiamine should be administered before administering glucose.</li> </ul>	Strong
<b>Other vitamins:</b> <ul style="list-style-type: none"> <li>- A multivitamin may be given intravenously each day (folic acid and pyridoxine).</li> <li>- Vitamin K addition is not necessary unless to treat a coagulopathy (add 150 mcg vitamin K).</li> </ul>	Conditional
<b>Antiemetics:</b> <ul style="list-style-type: none"> <li>- Begin with ondansetron 4 mg intravenously (IV push) once every eight hours upon hospitalization for intravenous fluid therapy and may increase to 8 mg IV every eight hours. After the patient has stabilized, ondansetron is discontinued.</li> </ul> <b>OR</b>	Strong

<ul style="list-style-type: none"> <li>- Intravenous dimenhydrinate 50 mg every four to six hours, metoclopramide 5 to 10 mg every eight hours, or promethazine 12.5 to 25 mg every four to six hours is an alternative to ondansetron.</li> <li>- Parenteral medications can be discontinued and oral medications started after 24 to 48 hours of gastrointestinal rest and when the patient is tolerating oral intake.</li> </ul>	
<p><b>Thromboprophylaxis:</b></p> <ul style="list-style-type: none"> <li>- Women admitted with HG should be offered thromboprophylaxis with low-molecular-weight heparin and those being managed as outpatients should be assessed for VTE risk.</li> <li>- Graduated compression stockings should be used when low-molecular-weight heparin is contra-indicated.</li> <li>- Thromboprophylaxis can be discontinued upon discharge providing no other indications exist for continuation of thromboprophylaxis.</li> </ul>	Strong
<b>Management of patients with refractory NVP and HG</b>	
Consider testing for H. pylori infection in patients unresponsive to standard therapy, who have symptoms beyond the first trimester, who require multiple hospitalizations, or who have symptoms of gastroesophageal reflux disease.	Conditional
<b>Enteral or parenteral nutrition</b>	
When all other medical therapies have failed to sufficiently manage symptoms, enteral tube feeding or parenteral nutrition should be considered with a referral to a specialized physician in clinical enteral and parenteral nutrition in parallel to ongoing medical therapies.	Strong
<b>Hospitalization</b>	
<p>Inpatient care should be considered if there is at least one of the following:</p> <ul style="list-style-type: none"> <li>- Continued nausea and vomiting and inability to keep down oral antiemetics.</li> <li>- Continued nausea and vomiting associated with clinical dehydration or weight loss (greater than 5% of body weight), despite oral antiemetics.</li> <li>- Confirmed or suspected comorbidity (such as urinary tract infection and inability to tolerate oral antibiotics).</li> <li>- Comorbidities such as epilepsy, diabetes, HIV, hypoadrenalism or psychiatric disease where symptoms and inability to tolerate oral intake and medication could present further complications.</li> </ul>	GPS
<b>Antenatal care after hospital discharge</b>	
<p>Women should only be discharged once:</p> <ul style="list-style-type: none"> <li>- Appropriate antiemetic therapy has been tolerated.</li> <li>- Adequate oral nutrition and hydration have been tolerated.</li> <li>- Management of concurrent conditions is completed.</li> </ul>	GPS
At the time of discharge, it is essential that women are advised to continue with their antiemetics for at least one week and that they know how to access further care.	Strong
Women with severe NVP or HG who have continued symptoms into the late second or the third trimester should be offered serial scans to monitor fetal growth.	Strong
<b>Long-term effects of NVP and HG on women</b>	
There is no evidence of significant impact on long-term all-cause mortality.	Strong
Women who experience HG in pregnancy are at increased risk of PND, anxiety, and PTSD	Strong
Women with previous HG should be advised that there is a risk of recurrence in future pregnancies.	Strong

<b>Future pregnancies</b>	
Early use of lifestyle/ dietary modifications and antiemetics that were useful in the index pregnancy is advisable to reduce the risk of NVP and HG in the current pregnancy	Strong

## Introduction

NVP affects up to 90% of pregnant women (1) and is one of the most common indications for hospital admission among pregnant women, with typical stays of between three and four days (2). NVP is defined as the symptom of nausea and/or vomiting prior to 16 weeks of gestation without other causes. (3) HG is a severe form of NVP, which affects between 0.3 and 3.6% of pregnant women, interfering with quality of life and the ability to eat and drink normally. Reported HG recurrence rates vary, from 15.2% to 89% if using self-reported diagnosis. (4) In a population-based pregnancy cohort using general practice records prevalence of clinically recorded NVP/HG was 9.1%: 2.1% had hospital admissions, 3.4% were treated with antiemetics in primary care only, and 3.6% had only recorded diagnoses. (5) The major mechanism of NVP and HG has recently been elucidated to be related to hypersensitivity to the vomiting hormone growth differentiation factor-15 (GDF15). GDF15 caused loss of appetite, taste aversion, nausea, vomiting and weight loss. hCG is unlikely to be causative. (6) Prevalence data specifically for general NVP in Egypt is limited, but studies showed that severe NVP and HG occurs in 0.5% to 2% of all pregnancies and result in a high hospital rate of 4.5% in some regions (7), which is considered high compared to universal figures.

## Scope and Purpose

The objectives of this guideline are:

- To provide guidance for the appropriate diagnosis and management of women with NVP and HG.
- To optimize outcomes for patients who are at risk of or developed NVP and HG.

## Target Audience

This guideline targets; healthcare professionals working as Obstetricians & Gynecologists, nurses, physicians working at emergency units, policy makers, hospital managers, and other stakeholders to apply the best practice and afford the most appropriate tools for women at risk of or having, ectopic pregnancy and pregnancy of unknown location

## Methodology

A comprehensive search for guidelines was done to identify the most relevant ones to consider for adaptation. The inclusion/exclusion criteria that were followed in the search and retrieval of guidelines to be adapted are:

**We select guidelines only if they are:**

- Evidence-based guidelines
- National and/or international guidelines
- Guidelines published from 2016 to 2025
- Peer reviewed publications
- Guidelines written in English language

**We Exclude guidelines that are:**

- Written by a single author not on behalf of an organization as guideline to be valid and comprehensive ideally requires multidisciplinary input.

- Published without references as the panel needs to know whether a thorough literature review was conducted and whether the current evidence was used in the preparation of the recommendations.

**The following characteristics of the retrieved guidelines were summarized in a table:**

- Developing organisation/authors
- Date of publication, posting, and release
- Country/language of publication
- Dates of the search used by the source guideline developers

All retrieved Guidelines were screened and appraised using AGREE II instrument ([www.agreetrust.org](http://www.agreetrust.org)) by at least three members. The panel decided on a cut-off point or ranked the guidelines (any guideline scoring above 50% on the rigor dimension was retained).

**Guidelines used in the adaptation process:**

- 1- The Management of Nausea and Vomiting in Pregnancy and Hyperemesis Gravidarum (Green-top Guideline No. 69). BJOG. 2024;131:e1–e30. (8)
- 2- Lowe SA, Bowyer L, Beech A, Tanner H, Armstrong G, Marnoch C, Grzeskowiak L. Position Statement on the Management of Nausea and Vomiting in Pregnancy and Hyperemesis Gravidarum. The Society of Obstetric Medicine of Australia and New Zealand (SOMANZ), Updated October 2023. (9)
- 3- Nausea and Vomiting of Pregnancy. ACOG Practice Bulletin, Clinical Management Guidelines for Obstetrician–Gynecologists, Number 189, January 2018. (10)
- 4- Martinez de Tejada B, Vonzun L, Von Mandach DU, Burch A, Yaron M, Hodel M, Surbek D, Hoesli I. Nausea and vomiting of pregnancy, hyperemesis gravidarum. European Journal of Obstetrics and Gynecology 304 (2025) 115–120. (11)
- 5- Smith JA, Fox KA, Clark SM. Nausea and vomiting of pregnancy: Clinical findings and evaluation. Up To Date, Sep, 2025 (12)
- 6- Smith JA, Fox KA, Clark SM. Nausea and vomiting of pregnancy: Treatment and outcome. Up To Date, Aug, 2025 (13)

**Evidence assessment**

According to WHO Handbook for Guidelines, we used the GRADE (Grading of Recommendations, Assessment, Development and Evaluation) approach to assess the quality of a body of evidence, develop and report recommendations. GRADE methods are used by WHO because these represent internationally agreed standards for making transparent recommendations. Detailed GRADE information is available on the following sites:

- GRADE working group: <http://www.gradeworkinggroup.org>
- GRADE online training modules: <http://cebgrade.mcmaster.ca/>
- GRADE profile software: <http://ims.cochrane.org/revman/gradepro>

**Table 1: Quality and Significance of the four levels of evidence in GRADE:**

Quality	Definition	Implications
<b>High</b>	The guideline development group is very confident that the true effect lies close to that of the estimate of the effect	Further research is very unlikely to change confidence in the estimate of effect
<b>Moderate</b>	The guideline development group is moderately confident in the effect estimate: the true effect is	Further research is likely to have an important impact on confidence in the

	likely to be close to the estimate of the effect, but there is a possibility that it is substantially different	estimate of effect and may change the estimate
<b>Low</b>	Confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the true effect	Further research is very likely to have an important impact on confidence in the estimate of effect and is unlikely to change the estimate
<b>Very low</b>	The group has very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of the effect	Any estimate of effect is very uncertain

**Table 2; Factors that determine How to upgrade or downgrade the quality of evidence**

<b>Downgrade in presence of</b>	<b>Upgrade in presence of</b>
<b>Study limitations</b> – 1 Serious limitations – 2 Very serious limitations	<b>Dose-response gradient</b> + 1 Evidence of a dose-response gradient
<b>Consistency</b> – 1 Important inconsistency	<b>Direction of plausible bias</b> + 1 All plausible confounders would have reduced the effect
<b>Directness</b> – 1 Some uncertainty – 2 Major uncertainty	<b>Magnitude of the effect</b> + 1 Strong, no plausible confounders, consistent and direct evidence + 2 Very strong, no major threats to validity and direct evidence
<b>Precision</b> – 1 Imprecise data	
<b>Reporting bias</b> – 1 High probability of reporting bias	

### The strength of recommendations

The strength of a recommendation communicates the importance of adherence to the recommendation.

**Strong recommendations:** The GDG found that the desirable effects of adherence to the recommendation outweigh the undesirable effects. This means that in most situations the recommendation can be adopted.

**Conditional recommendations:** This means that the GDG found that there is:

- Greater uncertainty about the strength of evidence, or
- The recommendation may account for a greater variety in patient values and preferences, or
- The resource use makes the intervention suitable for some, but not for other locations.

Conditional recommendations **are still the best available evidence to date and** it can be adopted if it meets the conditions mentioned with it.

**Good Practice Statement:** Statements based on opinion of respected authorities, e.g. the RCOG, ACOG, and the guidelines development group.

## Recommendations

### Diagnosis of NVP and HG:

- NVP is diagnosed when onset is prior to 16 weeks of gestation and other causes of nausea and vomiting have been excluded. **Strong recommendation, very low-quality evidence (8)**
- HG can be diagnosed when symptoms start in early pregnancy, nausea and/or vomiting are severe enough to cause an inability to eat and drink normally and strongly limits daily activities of living. Signs of dehydration are contributory. **Strong recommendation, very low-quality evidence (8)**
- An objective and validated index of nausea and vomiting such as the Pregnancy-Unique Quantification of Emesis (PUQE) tool can be used to classify the severity of NVP and HG. **Conditional recommendation, low quality evidence (8)**
- Clinicians should be aware of the features in history, examination and investigation that allow NVP and HG to be assessed and for their severity to be monitored. **Strong recommendation, very low-quality evidence (8)**
- Ketonuria is not an indicator of dehydration in pregnancy and should not be used to assess severity. **Strong recommendation, moderate quality evidence (8)**

### Evaluation:

The standard initial evaluation of pregnant individuals with persistent nausea and vomiting includes:

- Weight.
- Orthostatic blood pressure measurement.
- Heart rate.
- Ultrasound for confirmation of fetal viability, examination for fetal number or presence of a molar pregnancy (if not previously performed).
- Laboratory tests:
  - Laboratory evaluation is indicated in patients with persistent nausea and vomiting to determine the severity of disease, assess the patient's volume/metabolic status, identify or exclude other diagnoses that could account for the symptoms, and guide replacement therapy.
  - The standard initial basic evaluation of all pregnant patients with persistent nausea and vomiting includes: serum electrolytes urine ketones and specific gravity.
  - Based on the severity of disease and associated signs and symptoms, clinician may order a comprehensive metabolic panel or selectively order one or more of these tests: Blood urea nitrogen, creatinine, complete blood count, liver chemistries amylase/lipase phosphorus, magnesium, and calcium levels, albumin and thyroid function tests.
- Hepatic ultrasound is indicated if liver disease is suspected.
- Graded compression ultrasonography of the appendix is indicated if appendicitis is suspected.
- Additional laboratory testing or imaging should be considered for patients who are refractory to standard therapy or in whom another cause of symptoms is suspected. **(9 - 12)**

**Spectrum of findings and interpretation** — Laboratory abnormalities that can be caused by nausea and vomiting of pregnancy include:

- Electrolyte and acid-base derangements, such as hypokalemia and hypochloremic metabolic alkalosis (from vomiting gastric secretions). Ketosis can occur if caloric intake is minimal. (12, 13)
- An increase in hematocrit, which indicates hemoconcentration due to plasma volume depletion. The degree of hemoconcentration may be masked by the physiologic decline in hematocrit that normally occurs in pregnancy, although this is maximal in the second trimester. Lymphocyte count tends to be higher in patients with hyperemesis. (14)
- Elevated blood urea nitrogen and urine specific gravity are other signs of hypovolemia. The serum creatinine concentration will increase only if the degree of hypovolemia is sufficiently severe to reduce the glomerular filtration rate. (12)
- Abnormal liver chemistries occur in approximately 50% of patients who are hospitalized with hyperemesis gravidarum (15). The most striking abnormality is an increase in serum aminotransferases. Alanine aminotransferase (ALT) is typically elevated to a greater degree than aspartate aminotransferase (AST). The degree of abnormality in liver chemistries correlates with the severity of vomiting. (12)
- Elevated serum amylase and lipase occur in 10% to 15% of patients and the levels may increase as much as fivefold (as opposed to a 5- to 10-fold increase in acute pancreatitis). (16)
- Gestational transient hyperthyroidism occurs in 3% to 11% of cases in early pregnancy. (17) This is likely due to high serum concentrations of human chorionic gonadotropin, which has TSH receptor stimulating activity. (18) It is a temporary condition that resolves spontaneously without treatment. Complete resolution of biochemical hyperthyroidism usually occurs by 18 weeks of gestation as the symptoms of nausea and vomiting improve. (19, 20) Obstetric outcomes are not affected by this transient hyperthyroid condition. Expectant management of patients with hyperemesis gravidarum and gestational transient hyperthyroidism typically leads to a decrease in serum-free T4 levels in parallel with a decrease in hCG levels after the first trimester. (21) Thus, it is unnecessary to routinely measure thyroid function in patients with hyperemesis gravidarum unless they have overt signs or symptoms of hyperthyroidism. (22)
- Hypomagnesemia and hypocalcemia. Marked dietary deprivation can lead to progressive magnesium depletion. Magnesium depletion can cause hypocalcemia by producing parathyroid hormone (PTH) resistance, which occurs when serum magnesium concentrations fall below 0.8 mEq/L (1 mg/dL or 0.4 mmol/L) or by decreasing PTH secretion, which occurs in patients with more severe hypomagnesemia. (12)

#### **Nonpharmacologic therapies:**

- Avoid an empty stomach at all times, with small and frequent meals every 1–2 h. **Strong recommendation, very low-quality evidence (11)**
- Prevent a full stomach (i.e not mixing solid with liquid, avoiding large meals). **Strong recommendation, low quality evidence (11)**
- Eat dry food, high-protein snacks, and crackers in the morning before arising. **Strong recommendation, moderate quality evidence (11)**
- Avoid strong tasting and spicy food, eliminate supplemental iron. **Strong recommendation, moderate quality evidence (11)**
- Ginger, has shown a beneficial effect in reducing nausea symptoms, but not in reducing vomiting. **Strong recommendation, high quality evidence (11)**

- Acupuncture and acupressure at P6 or Neiguan point (located three finger breadths below the wrist on the inside of the wrist between the two tendons) have not been proven to significantly reduce nausea and vomiting. **Strong recommendation, high quality evidence (11)**
- Use of hypnosis for NVP found no good quality clinical evidence for its' efficacy. **Strong recommendation, high quality evidence (11)**

#### Pharmacological therapies:

- Combinations of different drugs should be used in women who do not respond to a single antiemetic. **Strong recommendation, (8)**
- For women with persistent or severe HG, non-oral routes may be necessary and more effective than an oral regimen. **Conditional recommendation, Low-quality evidence, (8)**

#### Stepwise approach for mild and moderate NVP without hypovolemia:

- **Step 1:** Doxylamine/pyridoxine (vitamin B6) is recommended as the first-line therapy for mild-moderate NVP: Doxylamine/pyridoxine 20/20mg PO at night, increase additional 10/10 mg in morning and 10/10mg at lunchtime if required. **Strong recommendation, moderate quality evidence (8)**

#### Rationale:

- Treatment of nausea and vomiting of pregnancy with vitamin B6 (pyridoxine) alone or vitamin B6 (pyridoxine) plus doxylamine in combination is safe and effective and should be considered first-line pharmacotherapy. However, pyridoxine alone is not available in Egypt up till now
- Vitamin B6 (pyridoxine) 10–25 mg orally (either taken alone or in combination with Doxylamine 12.5 mg orally) 3 or 4 times per day. Adjust schedule and dose according to severity of patient's symptoms. **OR**
- Vitamin B6 (pyridoxine) 10 mg/Doxylamine 10 mg combination product, two tablets orally at bedtime initially, up to four tablets per day (one tablet in the morning, one tablet in midafternoon, and two tablets at bedtime). **OR**
- Vitamin B6 (pyridoxine) 20 mg/Doxylamine 20 mg combination product, one tablet orally at bedtime initially, up to two tablets per day (one tablet in the morning and one tablet at bedtime). **(23, 24)**

#### Step-2: If no adequate response, ADD antihistaminic (H1 antagonists).

- Cyclizine 50 mg PO, IM or IV 8 hourly. **(8, 13) OR**
- Promethazine 12.5–25 mg 4–8 hourly PO (safest and preferred route of administration), IM or IV. Promethazine is primarily an H1 receptor-blocking agent, but it is also a weak dopamine antagonist. **(25, 26) OR**
- Meclizine 25 mg orally every four to six hours, as needed. **(27) OR**
- Diphenhydramine 25 mg can be given orally, intravenously, or intramuscularly every four to six hours or 50 mg orally, intravenously, or intramuscularly every six to eight hours, as needed. If the patient is taking doxylamine, the total dose of diphenhydramine should not exceed 100 mg/day to reduce the risk of side effects. Alternatively, discontinue doxylamine if it was completely ineffective. **(28) OR**

- Dimenhydrinate 25 to 50 mg can be given orally every four to six hours, as needed. Otherwise, 50 mg is administered intravenously over 20 minutes or 50 mg is administered rectally (where available every four to six hours, as needed. If the patient is taking doxylamine, the total dose of dimenhydrinate should not exceed 200 mg/day to reduce the risk of side effects. **(29)**

**Step-3: If no adequate response, ADD dopamine antagonists.**

- Prochlorperazine 5–10 mg 6–8 hourly PO (or 3 mg buccal); 12.5 mg 8 hourly IM/IV; 25 mg PR every 12-24h. **(30) OR**
- Metoclopramide 5–10 mg 8 hourly PO, IV/IM/SC (ideally 30 minutes prior to meal and at bedtime). Intravenous doses of metoclopramide should be administered by slow bolus injection over at least 3 minutes to help minimise extrapyramidal side effects. **(26, 31) OR**
- Domperidone 10 mg 8 hourly PO; 30 mg 12 hourly PR. However, there is no information on its safety or efficacy for treatment of NVP. **(8)**

**Step-4: If no adequate response, ADD Serotonin antagonist** (selective antagonists at the 5-hydroxytryptamine-3 (5-HT<sub>3</sub>) serotonin receptor):

- Ondansetron 4 mg 8 hourly or 8 mg 12 hourly PO; 8 mg over 15 minutes 12 hourly IV; 16 mg daily PR (Women taking ondansetron may require laxatives if constipation develops). There is evidence that ondansetron is safe. Its use should not be discouraged if first line antiemetics are ineffective. Women can be reassured regarding a very small increase in the absolute risk of orofacial clefting with ondansetron use in the first trimester, which should be balanced with the risks of poorly managed HG. **(32, 33)**
- Granisetron, and Dolasetron can also be used but the experience in pregnancy is little. **(34)**

**Step-5: If no adequate response, ADD corticosteroids.**

- Hydrocortisone 100 mg twice daily IV and once clinical improvement occurs, convert to prednisolone 40–50 mg daily PO, with the dose gradually tapered (by 5-10 mg per week) until the lowest maintenance dose that controls the symptoms is reached (Corticosteroids should be reserved for cases where standard therapies have failed; when initiated they should be prescribed in addition to previously started effective antiemetics. **(35)**

Acid-reducing agents can be used as adjunctive therapy. In patients with heartburn/acid reflux and NVP. **Conditional recommendation, very low-quality evidence, (36)**

In women with severe NVP or HG, input should be sought from other allied professionals. **Conditional recommendation, very low-quality evidence, (8)**

Women with previous or current NVP or HG should consider avoiding iron-containing preparations if these exacerbate symptoms or consider alternative route of administering iron. **Conditional recommendation, very low-quality evidence, (36)**

Histamine type-2 receptor blockers or proton pump inhibitors may be used for women developing gastro-oesophageal reflux disease, oesophagitis or gastritis **Conditional recommendation, very low-quality evidence, (8)**

### Management of vomiting with hypovolemia:

- **Hospital admission** for close monitoring and ongoing treatment is appropriate for those with persistent inability to tolerate oral intake resulting in hypovolemia requiring intravenous replacement fluid, and failure of oral and/or intravenous antiemetic therapy. **Strong recommendation, very low-quality evidence, (37)**
- **The goal of inpatient management** is to restore oral intake to enable adequate hydration and nutrition and use of oral antiemetic therapy after discharge. The decision to admit versus discharge to home also needs to be individualized based on the patient's ability to access outpatient resources. **Strong recommendation, moderate quality evidence, (38)**
- **Fluid and electrolyte replacement:** Hypovolemia due to persistent vomiting and inability to tolerate fluids is often associated with electrolyte abnormalities. A baseline electrocardiogram is indicated in patients with electrolyte abnormalities requiring repletion. **Strong recommendation, very low-quality evidence, (39)**
- **Fluid replacement:** Aggressively rehydrate with up to 2 liters of IV crystalloid over two hours. Lactated Ringer's solution is preferred due to decreased incidence of acute kidney injury compared with normal or isotonic saline. **Strong recommendation, moderate evidence, (40)**
- After initial resuscitation, IV fluids can be titrated to maintain urine output of at least 100 mL/hour or continued at a rate of 125 to 150 mL/hour, with close monitoring of oral intake and urine production. Then switch to dextrose 5% in 0.45% saline with 20 mEq potassium chloride at 150 mL/hour for patients with normal potassium levels. **Strong recommendation, moderate quality evidence, (41)**
- Urea and serum electrolyte levels should be checked daily in women requiring intravenous fluids. **GPS**
- In patients with electrolyte imbalance, consult intensive care specialist to correct the imbalance.
- **Thiamine:** To mitigate the risk of Wernicke encephalopathy, 100 to 200 mg thiamine (vitamin B1) should be added to the initial fluid resuscitation and then daily thereafter while the patient is taking nothing-by-mouth or for two to three days in patients with oral intake. If Wernicke encephalopathy is suspected, treat with 200 to 500 mg IV every eight hours for 2 to 7 days, followed by 250 mg once daily for an additional 3 to 5 days, followed by maintenance therapy 100 mg daily until no longer at risk for deficiency. Thiamine should be administered before administering glucose. **Strong recommendation – very low-quality evidence, (42-44)**
- **Other vitamins:** A multivitamin may be given intravenously each day (folic acid and pyridoxine). Vitamin K addition is not necessary unless to treat a coagulopathy (add 150 mcg vitamin K). **Conditional recommendation, moderate quality evidence, (13)**
- **Antiemetics:**
  - Begin with ondansetron 4 mg intravenously (IV push) once every eight hours upon hospitalization for intravenous fluid therapy and may increase to 8 mg IV every eight hours. After the patient has stabilized, ondansetron is discontinued. **Strong recommendation, moderate quality evidence, (10).**
  - Intravenous dimenhydrinate 50 mg every four to six hours, metoclopramide 5 to 10 mg every eight hours, or promethazine 12.5 to 25 mg every four to six hours is an alternative to ondansetron. **Strong recommendation, moderate quality evidence, (10).**

- Parenteral medications can be discontinued and oral medications started after 24 to 48 hours of gastrointestinal rest and when the patient is tolerating oral intake. **Strong recommendation, moderate quality evidence, (10).**
- **Thromboprophylaxis:** Women admitted with HG should be offered thromboprophylaxis with low-molecular-weight heparin and those being managed in the community should be assessed for VTE risk. Graduated compression stockings should be used when low-molecular-weight heparin is contraindicated. Thromboprophylaxis can be discontinued upon discharge providing no other indications exist for continuation of thromboprophylaxis. **Strong recommendation, low-quality evidence, (8)**

#### **Management of patients with refractory NVP and HG:**

- Consider testing for H. pylori infection in patients unresponsive to standard therapy, who have symptoms beyond the first trimester, who require multiple hospitalizations, or who have symptoms of gastroesophageal reflux disease. **Conditional recommendation, low quality evidence, (45)**

#### **Enteral or parenteral nutrition:**

- When all other medical therapies have failed to sufficiently manage symptoms, enteral tube feeding or parenteral treatment should be considered with a referral to gastroenterology and a multidisciplinary approach in parallel to ongoing medical therapies. **Strong recommendation, very low-quality evidence, (8)**

#### **Hospitalization:**

- Inpatient care should be considered if there is at least one of the following:
  - Continued nausea and vomiting and inability to keep down oral antiemetics.
  - Continued nausea and vomiting associated with clinical dehydration or weight loss (greater than 5% of body weight), despite oral antiemetics.
  - Confirmed or suspected comorbidity (such as urinary tract infection and inability to tolerate oral antibiotics).
  - Comorbidities such as epilepsy, diabetes, HIV, hypoadrenalism or psychiatric disease where symptoms and inability to tolerate oral intake and medication could present further complications. **(GPS), (8)**

#### **Antenatal care after hospital discharge:**

- Women should only be discharged once:
  - Appropriate antiemetic therapy has been tolerated.
  - Adequate oral nutrition and hydration have been tolerated.
  - Management of concurrent conditions is completed. **GPS, (8)**
- At the time of discharge, it is essential that women are advised to continue with their antiemetics for at least one week and that they know how to access further care. **Strong recommendation, very-low quality evidence, (8)**
- Women with severe NVP or HG who have continued symptoms into the late second or the third trimester should be offered serial scans to monitor fetal growth, **Strong recommendation, moderate quality evidence, (8)**

**Long-term effects of NVP and HG on women:**

- There is no evidence of significant impact on long-term all-cause mortality. **Strong recommendation, moderate quality evidence, (8)**
- Women who experience HG in pregnancy are at increased risk of postnatal depression (PND), anxiety and post-traumatic stress disorder (PTSD). **Strong recommendation, moderate quality evidence, (46)**
- Women with previous HG should be advised that there is a risk of recurrence in future pregnancies. **Strong recommendation, moderate quality evidence, (8)**

**Future pregnancies:**

- Early use of lifestyle/ dietary modifications and antiemetics that were useful in the index pregnancy is advisable to reduce the risk of NVP and HG in the current pregnancy **Strong recommendation, moderate quality evidence, (8)**

**Clinical Quality Standards for Monitoring**

➤ Diagnosis & Early Detection	
QS.1	NVP is diagnosed when onset is prior to 16 weeks of gestation and other causes of nausea and vomiting have been excluded
QM.1	<b>Numerator:</b> Number of mothers diagnosed as NVP > 16 weeks <b>Denominator:</b> Total number of mothers diagnosed with NVP-HG
QM.2	<b>Numerator:</b> Number of mothers with NVP diagnosed as other medical conditions <b>Denominator:</b> Total number of mothers diagnosed with NVP-HG
QS.2	HG is diagnosed when symptoms start in early pregnancy, nausea and/or vomiting are severe enough to cause an inability to eat and drink normally and strongly limits daily activities of living (see the differential diagnosis of NVP in appendix).
QM.2	<b>Numerator:</b> Total number of mothers diagnosed as mild NVP <b>Denominator:</b> Number of mothers hospitalized with dehydration within 48h after 1 <sup>st</sup> visit

➤ Treatment	
QS.1	Doxylamine/pyridoxine (vitamin B6) is recommended as the first-line therapy for mild-moderate NVP: Doxylamine/pyridoxine 20/20mg PO at night, increase additional 10/10 mg in morning and 10/10mg at lunchtime if required.
QM.1	<b>Numerator:</b> Total number of women with HG treated with Doxylamine/pyridoxine <b>Denominator:</b> Total number of women diagnosed as HG
QS.2	Hospital admission for close monitoring and ongoing treatment is appropriate for those with persistent inability to tolerate oral intake resulting in hypovolemia requiring intravenous replacement fluid, and failure of oral and/or intravenous antiemetic therapy.
QM.2	<b>Numerator:</b> Total number of admitted women diagnosed as HG with dehydration/hypovolemia <b>Denominator:</b> Total number of women diagnosed as HG with dehydration/hypovolemia
QS.3	To reduce the risk of Wernicke encephalopathy, 100 to 200 mg thiamine (vitamin B1) should be added to the initial fluid resuscitation and then daily thereafter while the patient is taking nothing-by-mouth or for two to three days in patients with oral intake.
QM.3	<b>Numerator:</b> Total number of women admitted with HG and dehydration/hypovolemia given thiamine <b>Denominator:</b> Total number of women admitted with HG and dehydration/hypovolemia

## Updating of the guidelines

This guideline will be updated whenever there is new evidence.

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# Appendix-1

## Differential Diagnosis of Nausea and Vomiting of Pregnancy:

### *Gastrointestinal conditions:*

- Gastroenteritis
- Gastroparesis
- Achalasia
- Biliary tract disease
- Hepatitis
- Intestinal obstruction
- Peptic ulcer disease
- Pancreatitis
- Appendicitis

### *Conditions of the genitourinary tract:*

- Pyelonephritis
- Uremia
- Ovarian torsion
- Kidney stones
- Degenerating uterine leiomyoma

### *Metabolic conditions:*

- Diabetic ketoacidosis
- Porphyria
- Addison's disease
- Hyperthyroidism
- Hyperparathyroidism

### *Neurologic disorders:*

- Pseudotumor cerebri
- Vestibular lesions
- Migraine headaches
- Tumors of the central nervous system
- Lymphocytic hypophysitis

### *Miscellaneous conditions:*

- Drug toxicity or intolerance
- Psychologic conditions

### *Pregnancy-related conditions:*

- Acute fatty liver of pregnancy
- Preeclampsia

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## Appendix-2

### Pregnancy Unique-Quantification of Emesis (PUQE) score

	1 point	2 points	3 points	4 points	5 points
Duration of nausea in the past 12 hours	0	≤1 hour	2 to 3 hours	4 to 6 hours	>6 hours
Number of vomiting episodes in the past 12 hours	0	1 to 2	3 to 4	5 to 6	≥7
Number of episodes of dry heaves in the past 12 hours	0	1 to 2	3 to 4	5 to 6	≥7

Total score 4 to 6: mild nausea and vomiting of pregnancy. Total score 7 to 12: moderate nausea and vomiting of pregnancy. Total score ≥13: severe nausea and vomiting of pregnancy.

*Adapted from:*

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