FOGSI - ICOG

Good Clinical Practice Recommendations

GCPR

Nausea/Vomiting in Pregnancy (NVP)/ Hyperemesis Gravidarum (HG)

Convenor – Kiran Pandey Co-Convenor – Ashok Kumar

Mentors – Hrishikesh D Pai, Madhuri Patel, Laxmi Shrikhande

Advisors – Sanjay Gupte, Hema Divakar

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Co-ordinator – Surekha Tayade

MEDICAL EDUCATION COMMITTEE

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Fogsi Good Clinical Practice Recommendations

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METHODOLOGY

The core contributors of "Nausea Vomiting in Pregnancy/Hyperemesis Gravidarum" GCPR have framed the recommendations for the good clinical practice in Indian perspective after reading all the related recent literature, randomized trials, systemic or meta-analysis and guidelines of major international OBG societies and the document has been reviewed by national experts from FOGSI.

Grade Practice Recommendations

Grade	*Descriptor*	*Qualifying Evidence*	*Implications for Practice*
A	Strong recommendation	Level I evidence or consistent findings from the multiple studies of levels II, III, or IV	Clinicians should follow a strong recommendation unless a clear and compelling rationale for an alternative approach is sack present
B	Recommendation	Levels II, III, or IV evidence and findings are generally consistent	Generally, clinicians should follow a recommendation but should remain alert to new information and sensitive to patient preferences
C	Option	Levels II, III, or IV evidence, but findings are inconsistent	Clinicians should be flexible in their decision-making regarding appropriate practice, although they may set bounds on alternatives; patient preference should have a substantial influencing role

PURPOSE AND SCOPE

These recommendations for FOGSI GCPR have been developed for the assistance of obstetricians, consulting physicians, general practitioners, and postgraduates providing guidance, and recommendations for managing women presenting with hyperemesis in pregnancy.

Hyperemesis GCPR has been formulated in simple language but structured manner with easy adoptable flow charts and algorithms covering the topic completely from diagnosis, monitoring, and management protocol that are workable in day-to-day practice.

DISCLAIMER

The recommendation included here should not be viewed as being exclusive or other concepts or as covering all legitimate strategies. The suggestions made here are not meant to dictate but to define the standard protocol that fits most with minimal risk and can be adopted at the peripheral as well as the institutional level.

BACKGROUND

Nausea & Vomiting of Pregnancy (NVP), also called morning sickness, is quite a common ailment with an incidence of approximately 50–80%, whereas hyperemesis gravidarum (HG) accounts for 0.3–3.6% of cases.[1]

- The recurrence rate is high, ranging from 15–81%.[2]
- Symptoms get worsened in next pregnancy if there was history of mild-to-moderate symptoms in previous pregnancy.

Pathophysiology is not clearly understood but is a complex interaction of multiple factors involving hormonal, genetic, gastrointestinal, psychological, and sociocultural causes[3] **(Annexure 1)**.

How Diagnose is of NVP/HG Should Be Made?

- Nausea and vomiting during pregnancy is generally a diagnosis of exclusion based on its first occurrence in early pregnancy with gradual resolution over weeks.[4]
- Symptoms typically start at 5–6 weeks of gestation, peak at approximately 9–10 weeks, and usually subside by 16–20 weeks in 90% of women.

Patients who are presenting with mild symptoms are vitally stable and do not require laboratory evaluation, hospitalization, or outpatient treatment.[9]

Hyperemesis gravidarum is the severe end of the spectrum of nausea and vomiting of pregnancy.[10]

It is recommended to make a diagnosis of HG when patient presents with following symptoms[11] (GRADE A):
- Persistent/protracted pregnancy-related vomiting, or >3 times/day
- Weight loss >5% pre-pregnancy body or weight loss >3 kg
- Ketonuria unrelated to other causes
- Dehydration and electrolyte imbalance

(II) International consensus:[12]
- Symptoms start in early pregnancy (before 16 weeks)
- Nausea and/or vomiting is severe
- Patient unable to eat and/or drink normally
- Daily activities are severely restricted
- May have orthostatic hypotension

How Can Severity of NVP Be Assessed?

Pregnancy Unique-Quantification of Emesis (PUQE) index was devised to assess the severity of NVP during first trimester, and the score directly correlates with the quality of life, demonstrating the clinical utility of the index[13,14] (GRADE C).

The scoring system PUQE index has been recommended to be used in every patient presenting with NVP/HG as it aids in for mode of treatment to be instituted (oral/IV), type of drug regimen as well as to monitor the progress with treatment (GRADE C).

The PUQE index has been modified that includes symptoms over the preceding 24 hours, including a sense of well-being score that is associated with hydration status of the patient, especially over an extended duration of time (GRADE C) **(Annexure 2)**.

When the patient experiences NVP for the first time after 9–10+6 completed weeks period of gestation or with signs and symptoms such as—abdominal pain/tenderness other than mild epigastric pain after retching, fever, persistent headache, abnormal neurological examination, and palpable goiter, it becomes important as well as it is recommended to rule out *differential diagnosis like diabetic ketoacidosis, starvation ketoacidosis, acute pancreatitis, acute cholecystitis, hepatitis, and peptic ulcer.* (GRADE B) **(Annexure 3 and Fig. 1)**.

Recommendation: Practitioners should have adequate knowledge of the risk factors and possibilities of other etiologies in a patient presenting with persistent nausea and vomiting; therefore, a detailed workup may be required in such a case **(Annexure 4)**.

Patients presenting with:
- Weight loss
- Hypotension
- Tachycardia
- Decreased oxygen saturation
- Tachypnea
- Oliguria
- Signs of dehydration

  May need hospitalization for monitoring and further management.

Effects of Hyperemesis Gravidarum on Fetomaternal Outcome

- NVP/HG has no adverse effect on fetus well-being, although few studies have shown increased incidence of low-birth-weight babies.[15]
- It is appropriate to counsel and reassure the patients that NVP/HG portends well for fetal outcome.
- Ithough very rare, Wernicke's encephalopathy, permanent neurological disability, splenic avulsion, esophageal rupture, and acute tubular necrosis have been reported in mother.[17,18]

PREVENTION—Recommendation:
- Women with previous history of HG should be counseled about the recurrent risk of future pregnancy (GRADE B).

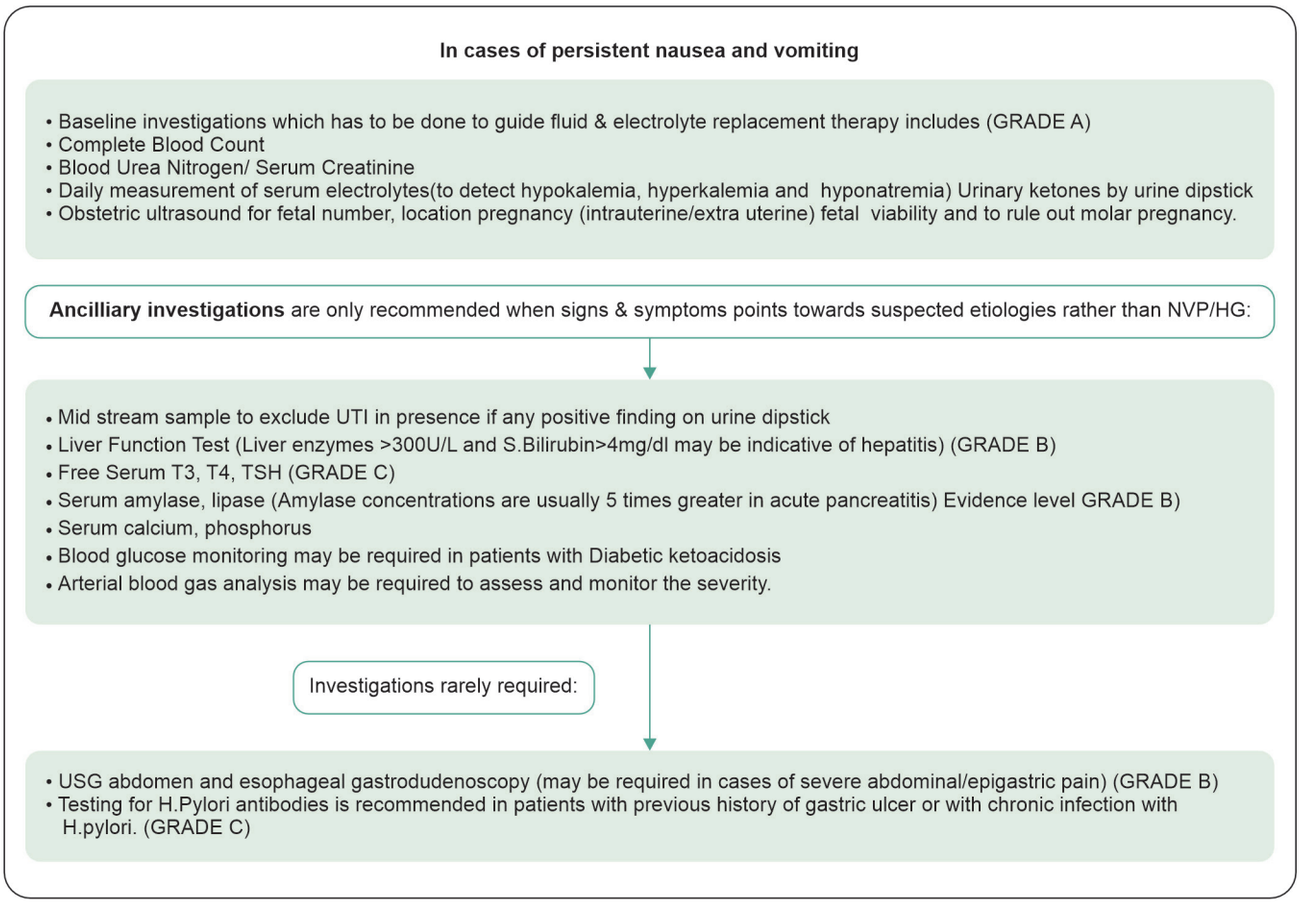

Fig. 1: Stepwise approach/investigation to be done in cases of persistent nausea and vomiting to rule out the causative factor

- It is recommended to take vitamin B1, vitamin B6, vitamin B12, and folic acid for 1 month prior to pregnancy as it is associated with decreased incidence of the N/V in pregnancy (GRADE A).
- Intake of vitamins may lead to correction of preexisting trace elements deficiency as well as increase in vitamin B6 levels, which help in alleviation of symptoms of NVP.
- Dietary as well as lifestyle modifications and use of antiemetics that were useful in previous pregnancy is also advisable in the current pregnancy for reducing the risk (GRADE C).
- Pregnant patients at higher risk for NVP may benefit from early administration of doxylamine and pyridoxine at the onset of pregnancy.

Practice recommendations for management of NVP/HG:

- Attitude of the pregnant female toward the severity of her symptoms, along with the effect of treatment on her fetus, may affect her clinical decision-making.
- It is recommended to institute early treatment of NVP to prevent progression to severe disease (GRADE C).
- Management includes conservative measures, non-pharmacological/complementary measures, and pharmacological interventions, which should be used in a graded manner depending upon the severity of symptoms, frequency, persistence of vomiting episodes, and associated complications, along with period of gestation.

Conservative measures:

- Following dietary changes are advisable:[19]
  - It is recommended to have frequent small meals at an interval of 1–2 hours to avoid full stomach (GRADE C).

  - It is recommended to have intake of dry snacks (rich in protein)/bland foods before getting up from the bed (GRADE C).
  - Foods with low fat and carbohydrate content should be preferred (GRADE C).
  - Spicy foods as well as foods with a strong odor should be avoided (GRADE C).
- Lifestyle modifications and avoidance of triggering factors, which are as follows:
  - Appropriate rest is recommended for an adequate sleep.
  - Triggering factors, such as close packed rooms, strong perfumes, smoke, heat, humidity, excessive noise, and dazzling lights, should be avoided.[20]
  - Iron tablets need to be stopped (GRADE C).

Complementary medicine: Probiotic supplementation in early pregnancy significantly reduced the severity of nausea, vomiting, and constipation and improves the quality of life (Grade B).

Non-pharmacological: In alternative medicine, the use of Ginger,[21] Chamomile, Cardamomum, Pomegranate, Spearmint, and lemon have been mentioned. At some places, the role of Aromatherapy, Acupuncture,[22-24] Hypnotic therapy, and Mindfulness-based cognitive therapy have also been mentioned, *but presently not recommended*.

Pharmacological Interventions:
Recommendations while prescribing pharmacological treatment of NVP

- The type, dose, and duration of drug therapy are decided on the basis of severity of symptoms, i.e., PUQE score.
- The teratogenicity of the drug should be taken into account while prescribing, especially in the first trimester, as this is the period of organogenesis.
- The dosing of the drug is increased gradually in titration with the severity of symptoms and the addition of another drug to the therapy should only be considered when there is persistence of symptoms.
- Change of drug whenever required should be done taking into account the tolerability as well as its side effects.
- Combinations of drugs from different classes are recommended in females who are unresponsive to first-line single antiemetic treatment because different drug classes may have different mechanisms of action, therefore causing different synergistic effects (GRADE C).
- In cases of intolerability to oral medications, route such as IV, rectal suppository, transdermal patch, or mouth dissolving formulation may be beneficial.
- History should always be taken about the previous drug reactions to antiemetic therapies before initiation of therapy in the current pregnancy.

Mi ld D isease[25-27] (PUQE score <7) **(Annexure 5)**:

- Treatment with pyridoxine (10–2 5 mg orally 8 hourly, max 100 mg/day) is recommended (GRADE A)
- Extended release of pyridoxine (Vit B6) (10 mg) + doxylamine (40 mg) medication have been approved by FDA, which is being extensively used in patients with mild NVP as it is both safe and effective.
- It should be considered as a first-line pharmacotherapy not responding to non-pharmacological and lifestyle intervention (GRADE A).
- The combination is not associated with maternal side effects, although sleepiness and drowsiness have been reported in 28% of patients (GRADE A).

Moderate Symptoms (PUQE score 7–12):

- Treatment as above along with addition of:
  Antihistaminic (H1 receptor antagonist—promethazine, cyclizine, cinnarizine, dimenhydrinate) and phenothiazine (prochlorperazine, chlorpromazine).
  They are considered safe and should be prescribed in patient presenting with moderate symptoms (GRADE A).
- Dopamine receptor antagonists—metoclopramide (5–10 mg orally TDS Max: 30 mg/day 1.2 mg/hour IV/IM).
- Although metoclopramide is safe and effective but because of risk of extrapyramidal side effect (increased muscle tone with involuntary motor activity) it has been recommended to be used as second-line antiemetic if the patient is unresponsive to H1 receptor antagonist and phenothiazine (GRADE B)
- It should be immediately stopped if the patient presents with extrapyramidal symptoms (GRADE B).

SEVERE SYMPTOMS (PUQE score >13)
Serotonon 5—hydroxytryptaminie type 3 receptor antagonist:

- Ondansetron (Serotonin 5HT3 inhibitor) 4 mg orally or IV is safe and effective, but few studies have demonstrated a very small risk of teratogenicity; therefore, it should be avoided in the first trimester (GRADE B).
- FDA recommends that ondansetron should not be used IV in a dose >16 mg/day as there is potential risk of QT interval prolongation leading to fatal heart rhythm.
- Electrolyte and ECG monitoring are recommended during treatment with ondansetron (IV dose) for patients who have risk factors for arrhythmia (GRADE C).

Corticosteroid:

- Use of corticosteroids is recommended when the patient is refractory or unresponsive to standard therapies but should be avoided in first trimester (Level B).
- Dosing of corticosteroids:
  - Hydrocortisone 100 mg IV BD or prednisolone 16 mg IV TDS for 2–3 days or oral dose of methyl prednisolone 40–50 mg.
  - Dose needs to be tapered in 2 weeks according to resolution of symptoms.
  - Patients who do not response within 3 days of treatment are not likely to respond, and therefore the cessation of treatment is recommended (GRADE A).

Patients presenting with refractory or unretractable nausea & vomiting require hospitalization. Indications are as follows (GRADE B):

- Patients with s/s of dehydration & intolerant to oral rehydration treatment or unable to tolerate oral antiemetics.
- Patients with s/s of moderate ketonuria (3–4+ve) or >5% of weight loss, electrolyte disturbances, or nutritional deficiencies.
- Patients with suspected or confirmed comorbidity.

- Assess vitals 2 hourly, with documentation on standard observation chart.
- In patient with severe NVP a multidisciplinary approach requires nutritionist physician, endocrinologist (GRADE C).

Practice recommendation for intravenous fluid therapy:

- Amount and type of fluid therapy should be guided by the degree of dehydration and the consideration of electrolyte imbalances.
- Common types of fluid used for fluid replacement are isotonic solutions like normal saline and Hartman's solutions and both are equally effective in treating complications of hyperemesis gravidarum.
- Given that most women admitted to hospital with HG are hyponatremic, hyperchloremic, and hypokalemic and ketotic, it seems appropriate to use normal saline and potassium chloride (Level C) (ANNEXURE 6).
- Correction of ketosis and vitamin deficiencies are recommended (Level C).
- Dextrose saline infusions are not recommended unless serum Na level returned to normal to prevent Wernikes encephalopathy[28] (Level C).
- In cases of severe hyponatremia, serum sodium should not be corrected faster than 10 mmol/L per 24 hours to prevent central pontine myelinolysis.
- Thiamine 100 mg should be given IV first, to prevent Wernicke's Encephalopathy[28] (Level C).
- Serum electrolyte levels & serum urea should be checked daily, and replacement should be done accordingly until intravenous fluid is given (Level C).
- Rapid Hydration:[29]
  - The rate of rehydration depends on the severity of NVP but usually aggressive rehydration with 1 liter of 0.9% saline with 20 mmol potassium chloride (KCl) over 2 hours is often appropriate (ANNEXURE 7) followed by 1 liter of 0.9% sodium chloride over 2–4 hours.
  - If Na is <125 mmol/L treatment should be considered in consultation with a physician.
- Infusions rates for fluid replacement should run at a minimum of 1 liter of fluid over 4–6 hours in first 24 hours.
- The composition of further fluid therapy given will depend upon the patient's serum electrolyte values.
- Allow water to moisten the mouth **(Fig. 2)**.

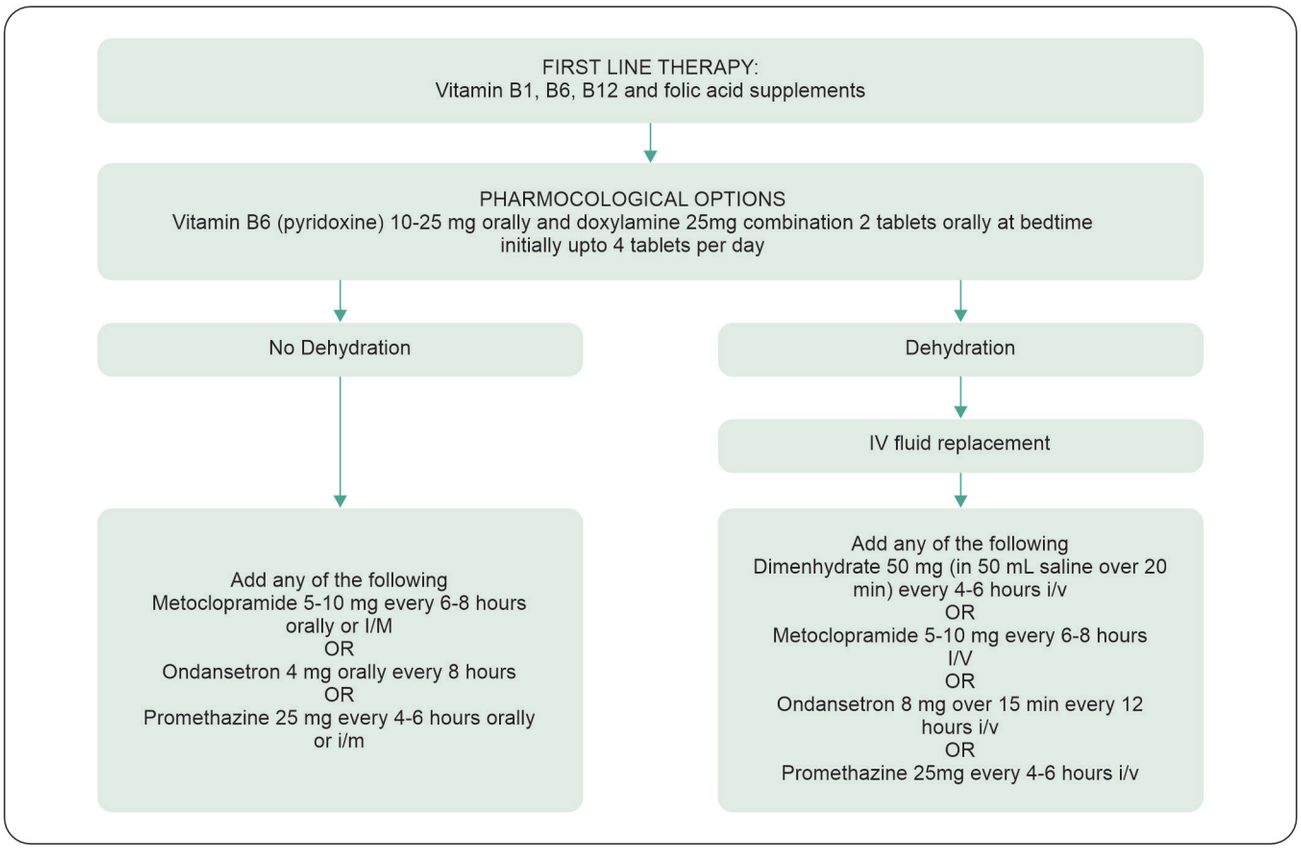

Fig. 2: Stepwise pharmacological approach towards NVP/HG

When the patients show the following signs of clinical improvement, she can be discharged:

- Re-check urinary ketones after 2 L of IV fluid replacement. If 2+ or less and with no tachycardia (>100 bpm) or temp >37.5°C, the patient can be discharged.
- Adequate urine output (0.5 mL/kg/hour).
- If the woman is tolerating 2 meals without vomiting.
- Encourage fluid and food intake in small frequent amounts.
- When the patient is being discharged, following advices are recommended.
- Management plan should be tailored according to patient symptoms (GRADE B).
- Continue oral antiemetics.
- Counseling regarding dietary changes and lifestyle modifications should be done along with psychological care and support.

Refractory cases:

When the patient is refractory to all possible medical therapies, enteral or parental treatment may be considered with a multidisciplinary approach (Level C).

General considerations:

- Antacids may be considered in the treatment of NVP during pregnancy, if the patient complains of gastroesophageal reflux (heartburn) or gastritis.
- Antacids syrups with calcium and aluminum ingredients are safe, whereas bismuth and bicarbonates can have adverse effects.

- H2 receptor antagonists or Proton Pump inhibitors (Lansoprazole, Pantoprazole 30–40 mg IV or orally empty stomach) have good safety profile and may be used for women having GERD (GRADE C).
- H. pyroli treatment is recommended in patients who are resistant to standard therapy (antibiotics with H2 receptor antibiotics) (GRADE C).
- Thromboprophylaxis with LMWH is recommended in women who are admitted to the hospital with prolonged history of hyperemesis gravidarum unless they are contraindications and should be discontinued on discharge (GRADE C).

The following Algorithm showing stepwise management of NVP/HG:

EXECUTIVE SUMMARY

- NVP/HG is a clinical diagnosis of exclusion, presents in the first trimester before 9 weeks and affects almost 70% of the pregnant population.
- Hyperemesis Gravidarum is the extreme or severest form of nausea and vomiting of pregnancy spectrum (**Grade A**).
- PUQE index/score is a useful and validated tool to determine the clinical severity as well as aid in the decision-making with respect to inpatient and outpatient as treatment and the regimen to be focused (**Grade C**).
- It is important to rule out surgical causes of acute abdomen (acute cholecystitis, appendicitis, and pancreatitis) is cases of unusual presentation, especially in second trimester (**Grade B**).
- Lifestyle and Dietary changes such as avoidance of fat-rich spicy food and high carbohydrate content while bland snacks and high protein content are preferable (**Grade C**).
- Combination of pyridoxine with doxylamine is considered as a first-line therapy rather than either monotherapy (**Grade A**).
- Combinations of drugs belonging to different classes that differ in mechanism of action will be used. Start with minimal effective dose and increase and titrate the dose according to response.
- H1 antihistamines and phenothiazines are considered in patients with mild to moderate NVP (**Grade B**).
- Metoclopramide should be used as a second-line antiemetic because of extrapyramidal side effects (**Grade B**).
- Ondansetron (5HT3 inhibitor) is safe in second trimester, and more than 16 mg/day IV should be avoided, especially in those with the potential risk of QT interval prolongation (**Grade B**).
- Glucocorticoids should be reserved for non-responsive and refractory cases, and treatment with these drugs should be avoided before first trimester (**Grade B**).
- Plain dextrose infusion should be avoided unless the serum sodium levels are normal and thiamine has been administered (**Grade C**).
- Thiamine supplementation of 100 mg (either oral or IV) should be given to women admitted with prolonged vomiting, especially before administration of dextrose or parentral nutrition (**Grade C**).
- When the patient is refractory to all possible medical therapies, enteral or parental treatment may be considered with a multidisciplinary approach (**Grade C**).

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ANNEXURE 1

Pathophysiology: It is not clearly understood but is a complex interaction of multiple factors involving hormonal, genetic, gastrointestinal, psychological, and sociocultural causes.[3]

- Pregnancy hormones such as hCG, estrogen, and progesterone are implicated in etiology (GRADE B).
- Increased severity may be caused by transient hyperthyroidism-like picture (raised free T4 & low TSH) (GRADE B).
- The risk of hyperemesis gravidarum is also increased due to gastroesophageal reflux disorders during pregnancy affecting the motility & sphincter relaxation.[4,5]
- Association with hepatic dysfunction, gastrointestinal dysrhythmias, overactivation of sympathetic system, lipid and immunological aberrations, and psychological stress are also being implicated (GRADE C).
- Helicobacter pylori infection has been associated with increased likelihood of HG.[6] (GRADE C)
- Genetic association with GDF15 (Growth differentiation factor 15), IGFBP7 (insulin growth factor binding protein 7) & RyR2 (ryanodine receptor 2) genes involved in placentation, appetite, cyclical vomiting, and cachexia has been notified, out of which GDF15 has been strongly implicated in both familial and recurrent cases of HG.[7] Familial history has been associated with 73% of cases, especially in first degree relatives.[8] (GRADE C)

ANNEXURE 2

PUQE INDEX showing the duration of nausea and the number of episodes and heaves.

	1 point	*2 points*	*3 points*	*4 points*	*5 points*
Duration of nausea in last 12 hrs	0	≤1 hr	2–3 hrs	4–6 hrs	>6 hrs
Number of vomiting episodes in last 12 hrs	0	1–2	3–4	5–6	≥7
Number of episodes of dry heaves in last 12 hrs	0	1–2	3–4	5–6	≥7

Mild: Score 4–6; Moderate: Score 7–12; Severe: ≥1 2

ANNEXURE 3

Table Differential diagnosis of NVP/HG15

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 Tumors of the central nervous system	**Miscellaneous conditions** Drug toxicity or intolerance Psychologic conditions	Pregnancy-relatedconditions Acute fatty liver of pregnancy Preeclampsia

Diagnosis of gestational transient thyrotoxicosis[16]

- No prior history of thyroid diseases No evidence of Graves' disease
- Self-limiting disease of emesis Increased FT4/decreased S. TSH
- Routine thyroid test is not indicated as management of Gestational Transient Thyrotoxicosis is supportive because it resolves spontaneously by 20 weeks POG. (GRADE B)
- Antithyroid drugs are not recommended. (GRADE B)

ANNEXURE 4

Risk Factors associated with NVP/HG (GRADE B)

- Young age
- Lower socioeconomic status
- Nulliparity
- Multiple pregnancy
- Molar pregnancy
- Extremes of BMI
- Asian or Black ethnicity
- History of thyroid and parathyroid dysfunction
- History of type-1 DM
- Trace element deficiencies
- Family history (IS degree relatives)
- Women with history of motion sickness, migraine, infertility, intolerance to oral contraceptives
- History of psychiatric or mood disorder

ANNEXURE 5

Various Non-Pharmacological/Pharmacological Agents Used for Management of NVP/H

Drug	*Action*	*Dose*	*Efficacy*	*Side effects*	*Teratogenic*	*Practical issues*
Ginger	Lower GI motility ↑,	250 mg 6 hrly max 1.2 mg	Nausea notvomiting, equal to B6 (LOE3)	Heartburn, poor tolerance	No	Risk of Theoretical bleeding as it ↓ platelet aggregation
Pyridoxine	↓ H1 & muscarine receptor and vestibular system	10–25 mg 3–4 times Max 200 mg	Less effective than dimenhydrinate	Sensory neuropathy if >500 mg	No	-
Doxylamine	Anti-histaminic H1 receptor antagonist Suppresses vomiting center & vestibular system	10–20 mg HS to 40 mg/day TDS in divided doses	Nausea ↓ with or without B6 (LOE2)	No adverse effects	No	Combination with pyridoxine is more effective. If not effective, stop doxylamine and switch to another antihistaminic. Avoid with ondansetron as combination leads to prolongation of QT interval
Diphenhydramine	Antihistaminic H1 receptor antagonist	25–50 mg 8–6 hourly, IV 10–50 mg Max 150 mg/day	↓ NVP	Sedation anticholinegic	Not significant	It is a second-line agent. Sedative, therefore should be avoided in day time if >1 week usage is desired. Avoid with ondansetron. Often combined with caffeine
Dimenhydrinate	HI receptor antagonist	25–50 m 8–6 hourly, max 200 mg IV 10–50 mg over 20 min	Same as diphenhydramine	Sedation	Not reported	As travel sickness tablet
Metoclopramide	Dopamine serotonin receptor inhibitor, CNS-suppresses vomiting center	5–10 mg TDS orally IM IV 1.2 mg/hr Max30 mg/day	As effective as promethazine 25 mg	Long use risk of movement disorder Tardivedyskinesia	No	Prescribe 30 min before meals Combination with pyridoxine or with Diphenhydramine is better than alone
Promethazine	Antiemetic effect by early emptying of stomach	12.5, 25 mg 8–6 hourly max 75 mg, IM Avoid IV	Same as metoclopramide	Sedation Dystonic reaction IV risky	Potential risk of neonatal RDS which is unlikely in early gestation	Avoid IV as intra-arterial risk of gangrene in arm, subcutaneousrisk of tissue necrosis

Contd...

Contd...

Drug	*Action*	*Dose*	*Efficacy*	*Side effects*	*Teratogenic*	*Practical issues*
Prochlorperazine	Central and peripheral dopamine antagonist	5–10 mg, orally, IV, IM every 8–6 hrly 25 mg BD rectally	Superior to Placebo LOE 1	Dizziness, drowsiness , headache, Extrapyramidal	Casereports of congenital malformation Large series have not reported	Serious side effects rare Potential risk of QT prolongation Best reserved for evening dose
Chlorpromazine	As above	10–25 mg TDS	Superior to placebo	Same as above	Not reported	Not recommended by ACOG
Ondansetron	Serotonin antagonist 5HT3 antagonist	4.8 mg TDS	Superior to Doxylamine +B6 and metoclopramide	Constipation headachedizziness	Small study risk of oral	Only in cases refractory when drugs two combinations fail Avoid to use in <10 weeks
Glucocorticoids	Antiemetic by ↓ chemoreceptor trigger in brainstem	Prednisolone 40–50 mg/day Hydrocortisone 100 mg IV BD or Methylprednisolone 16 mg IV 8 hrly for 48–72 hrs, after IV orally 40–50 mg and taper in 7–10 days	Equal to promethazine	Mood disturbances Hypertension Hyperglycemia Cushing's	Risk of oral cleft	Restricted for refractory cases. Avoid in first trimester Wean over 7–10 days,minimal dosageshould be used until symptoms resolve

ANNEXURE 6

Composition of various fluids

Lactate component in RL was not proven to worsen the starvation amongst patients with Hyperemesis Gravidarum.

	Na (mmol/L)	*K (mmol/L)*	*Ca (mmol/L)*	*Cl (mmol/L)*	*Dextrose*	*Lactate (mmol/L)*
Ringer'slactate	131	5	2	111	-	29
NaCl (0.9%)	154	-	-	154	-	-
NaCl & Dextrose (0.9% & 5%)	154	-	-	154	5 gm/100 mL	-
Dextrose (5%)	-	-	-	-	5 gm/100 mL	-

ANNEXURE 7

Type of Fluid to Be Given Depending upon Serum Potassium Levels

- If K+ normal: One liter of Ringers lactate over 2 hours
- If K+ (3.5–3.9 mmol/L): One liter of 0.9% Sodium Chloride with 20 mmol/L through infusion pump at 500 mL per hour
- If K+ (3.2–3.4 mmol/L): 0.9% Sodium Chloride with K+ 40 mmol/L through infusion pump at 250 mL per hour
- Second liter of 0.9% Sodium Chloride or Hartmann's over 4 hours
- If K+ < 3.2 mmol/L: (1L 0.9% saline + 40 mmol k+, 3L/day)

Disclaimer-These recommendations for "Nausea/Vomiting in Pregnancy (NVP)/Hyperemesis Gravidarum (HG)" have been developed, to be of assistance to obstetricians, gynecologists, consulting physicians and general practitioners by providing guidance and recommendations for managing women with anemia and suffering from hemorrhagic conditions. The recommendations included here shouldn't be viewed as being exclusive of other concepts or as covering all legitimate strategies. The suggestions made here are not meant to dictate how a particular patient should be treated because they neither set a standard of care nor do they guarantee a particular result. To diagnose patients, choose dosages, and provide the best care possible while also taking the necessary safety precautions, clinicians must rely on their own experience and knowledge. The writers or contributors disclaim all responsibility for any harm and/or damage to people or property resulting from the use or operation of any techniques, goods, guidelines, or ideas presented in this content.