Case report of hyperemesis gravidarum: Hormonal change due to pregnancy and hypothyroidism

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SUMMARY

Hyperemesis gravidarum (HG) is an extreme form of nausea and vomiting in pregnancy, often leading to severe dehydration, electrolyte imbalances, and significant weight loss, posing risks for both maternal and fetal health. In this report, we present a complex case of a 32-year-old woman at 16 weeks of gestation with HG complicated by suspected gastroparesis and subclinical hypothyroidism. The patient reported unrelenting nausea, vomiting over seven times daily, abdominal fullness, and a substantial weight loss of 8 kg. She exhibited symptoms of weakness, tingling in her limbs, and a three-day history of constipation, highlighting the debilitating nature of HG compounded by delayed gastric emptying. Laboratory results revealed mild anemia, electrolyte imbalances, and elevated TSH, indicating subclinical hypothyroidism. Imaging confirmed superficial gastritis and esophagitis, adding to the diagnostic complexity. Management included antiemetics, levothyroxine, and prokinetic agents, aiming to stabilize her condition and support nutritional intake. This case underscores the multifaceted approach required for HG management, particularly when concurrent conditions like gastroparesis and hypothyroidism are present. Early and accurate diagnosis is crucial to avoid complications such as malnutrition, intrauterine growth restriction, and preterm birth. A multidisciplinary approach, incorporating obstetric, endocrinological, and gastrointestinal care, is essential in optimizing outcomes for both mother and fetus. Through this case, we explore the interconnected pathophysiology of HG, gastroparesis, and hypothyroidism in pregnancy, highlighting the need for vigilant monitoring and personalized management to address the complex symptoms and prevent severe maternal-fetal outcomes.

INTRODUCTION

Hyperemesis gravidarum (HG) is a severe manifestation of nausea and vomiting in pregnancy, surpassing typical morning sickness in intensity and persistence. It is marked by excessive vomiting, dehydration, electrolyte imbalances, and substantial weight loss, affecting approximately 0.3–2% of pregnancies.[1] Early differentiation between HG and normal pregnancy-related nausea and vomiting is critical, as HG can lead to serious maternal and fetal complications. Gastroparesis may complicate HG due to its delayed gastric emptying, which can aggravate symptoms of nausea, vomiting, and early satiety.[2] Pregnancy-related hormonal changes, particularly increased progesterone levels, can exacerbate or trigger gastroparesis, complicating nutritional intake and management. Gastroparesis in pregnancy requires dietary adjustments, prokinetic agents, and careful monitoring to mitigate risks such as dehydration and malnutrition. Additionally, subclinical hypothyroidism may exacerbate symptoms such as fatigue, constipation, and nausea, complicating the differential diagnosis of gastrointestinal distress in pregnancy.[3] Thyroid hormone plays a vital role in metabolic and gastrointestinal regulation, and untreated subclinical hypothyroidism is associated with increased risks of preterm delivery, preeclampsia, and low birth weight.[2]

Management strategies for HG and associated conditions require a personalized, multifaceted approach, often including antiemetics, proton pump inhibitors, and sucralfate to control gastrointestinal symptoms. Hydration, electrolyte replacement, and, in severe cases, intravenous fluids are essential to address dehydration and prevent malnutrition. Nutritional support is a cornerstone of ensuring adequate intake and safeguarding fetal development and maternal health. Despite appropriate management, HG and its associated complications can lead to significant maternal and fetal risks. Maternal complications include dehydration, nutritional deficiencies, and electrolyte imbalances, which may result in further cardiovascular, renal, or metabolic issues if not carefully managed. Fetal complications are also of concern, particularly in cases of poorly controlled HG, as the condition can lead to intrauterine growth restriction (IUGR), preterm birth, and in some extreme cases, fetal death.[4]

The objectives of this case report are to highlight the clinical challenges and diagnostic complexities encountered in a pregnant patient presenting with hyperemesis gravidarum, suspected gastroparesis, and subclinical hypothyroidism. Specifically, the report aims to discuss the pathophysiology and differential diagnosis of severe pregnancy-related nausea and vomiting, explore the impact of coexisting conditions such as gastroparesis and hypothyroidism on management, and evaluate the therapeutic approach, including pharmacologic and supportive treatments.

CASE PRESENTATION

Investigation

A 32-year-old pregnant woman, currently at 16 weeks of gestation, presented with persistent nausea and vomiting that had progressively worsened over the past three days. She reported experiencing more than seven episodes of vomiting

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Table I. Laboratory Results Supporting the Diagnosis

Parameter	26/05/24	18/06/24	19/08/24	05/09/24	07/10/24	11/10/24	01/11/24	Notes/Interpretation
Hemoglobin (Hb)	11.9	12.3	11.8	12.1	11.7	10	11.7	Mild decrease in Hb, consistent with weight loss and possible malnutrition due to hyperemesis gravidarum.
Hematocrit (Hct)	36%	37.4%	36.2%	34.5%	35.8%	29%	36%	Decrease in hematocrit, potentially linked to dehydration or poor intake.
Leukocytes (WBC)	6.9	7.88	10.8	10.6	8.8	6.64	9.3	Slightly elevated WBC in some tests may indicate mild stress or infection.
Platelets (Plt)	236	300	297	304	269	222	282	Within normal range, no signs of significant bleeding or clotting abnormalities.
Sodium (Na)	140	140	136	134.5	-	131	134	Mild hyponatremia, possibly from dehydration due to vomiting and fluid loss.
Potassium (K)	3.3	4.1	4.3	3.5	-	2.8	3.3	Mild hypokalemia, potentially due to vomiting and electrolyte loss.
Random glucose levels	-	-	-	-	-	-	132	Elevated glucose level, likely due to stress, dehydration, and possible ketone production.
Urine: Protein	-	Neg	(+)1	(+)1	(+)2	-	(+)1	Proteinuria could indicate renal stress, possibly due to dehydration and hypovolemia.
Urine: Ketones	-	Neg	(+)4	(+)1	(+)4	-	(+)3	Elevated ketones, suggesting dehydration or prolonged fasting from vomiting.
TSH	-	-	-	-	-	-	5.1	Elevated TSH and normal FT4, indicating subclinical hypothyroidism, which may exacerbate symptoms of
FT4	-	-	-	-	-	-	1.25	hyperemesis gravidarum.

Table II: Differential Diagnoses and Respective Considerations

Diagnosis	Differential Diagnoses
Hyperemesis gravidarum	• Gestational trophoblastic disease: Ruled out by normal imaging and hCG levels. • Pancreatitis: Excluded by normal amylase and lipase levels. • Metabolic disorders: No metabolic acidosis or hallmark features. • Intestinal obstruction or infections: Imaging and endoscopy ruled out mechanical obstructions or infections.
Suspected gastroparesis	• Autonomic neuropathy: No diabetes or neurological history. • Mechanical obstruction: Excluded by imaging and endoscopy. • Medication-induced gastroparesis: No history of anticholinergic or opioid use.
Subclinical hypothyroidism	• Central hypothyroidism: Excluded by normal FT4 levels. • Euthyroid sick syndrome: Unlikely without signs of critical illness. • Transient gestational hypothyroidism: Less likely due to persistence beyond the first trimester.

per day, particularly after meals. Additional symptoms included abdominal fullness, intermittent abdominal pain, frequent belching, weakness, and tingling sensations in her limbs. Over the course of her pregnancy, she experienced a significant weight loss of 8 kg and had not had a bowel movement for three days.

The patient's medical history included chronic gastritis and a prior diagnosis of cholecystitis. She had been hospitalized multiple times for similar symptoms during previous pregnancies, initially attributed to normal pregnancy-related conditions. Previous interventions included treatments with antiemetics, proton pump inhibitors, and steroids, but these failed to alleviate her symptoms and instead led to progressive worsening.

On physical examination, the patient appeared dehydrated and malnourished, with a weight of 52 kg, a height of 168 cm, and a BMI of 18.4, indicating underweight status. Her vital signs were as follows: blood pressure 106/64 mmHg, respiratory rate 20 breaths per minute, heart rate 58–65 beats per minute, and axillary temperature 36.1°C.

Abdominal examination revealed a soft, non-distended abdomen with mild tenderness localized to the epigastric region. No guarding, rebound tenderness, or palpable masses were noted. Percussion was tympanic over the epigastric area, and auscultation revealed hypoactive bowel sounds, suggestive of delayed gastric emptying. Neurological evaluation identified slightly reduced motor strength (4/5) in the lower extremities, mild paresthesia in both hands and

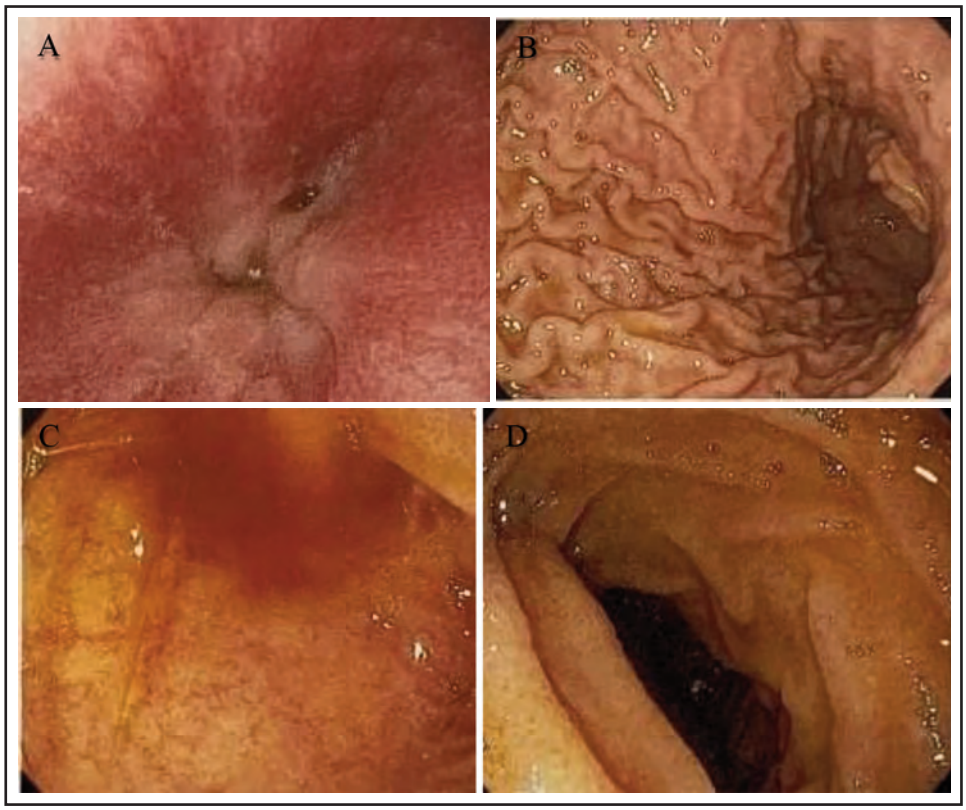

Fig. 1: Endoscopy Evaluation. A. hyperemic esophagus; B. hyperemic gaster; C. hyperemic bulbus of duodenum; D. hyperemic duodenum mucous

feet, and normal deep tendon reflexes. Other systemic findings included dry mucous membranes, reduced skin turgor, delayed capillary refill (3 seconds), and no edema in the extremities. Cardiovascular and respiratory examinations were unremarkable.

Laboratory tests revealed mild decreases in hemoglobin (Hb: 10–11.9 g/dL) and hematocrit (Hct: 29–37%), mild hyponatremia (131–140 mEq/L), and hypokalemia (2.8–4.3 mEq/L). Urinalysis showed positive ketones and proteinuria (+1 to +2), and random blood glucose was mildly elevated at 132 mg/dL. Thyroid-stimulating hormone (TSH) was elevated at 5.1 mIU/L, indicating subclinical hypothyroidism. Imaging and endoscopic evaluation demonstrated hyperemic mucosa in the esophagus, stomach, and duodenum, but no evidence of infection or malignancy.

From a psychosocial perspective, the patient expressed significant stress and anxiety related to her persistent symptoms and their potential impact on her ability to care for herself and her baby. Financial concerns and limited availability of her husband, due to work commitments, exacerbated her emotional burden. However, she reported some emotional and physical support from her mother. A family history revealed hypothyroidism in her mother and postpartum depression in a maternal aunt.

Diagnosis

The diagnostic process for this case involved a combination of physical examination, laboratory testing, urine analysis, imaging, and endoscopic evaluation. Physical examination (PE) findings indicated moderate dehydration, malnutrition (BMI: 18.4 kg/m^2), hypoactive bowel sounds suggestive of delayed gastric emptying, and mild paresthesia in the extremities. Laboratory results showed mild anemia, hyponatremia, hypokalemia, positive urine ketones and proteinuria, elevated random blood glucose, and an increased TSH level (5.1 mIU/L), consistent with subclinical hypothyroidism. Endoscopic findings revealed hyperemic mucosa in the esophagus, stomach, and duodenum, supporting the suspicion of gastroparesis but ruling out structural obstructions, malignancy, or infection.

The case was challenging due to persistent, severe vomiting refractory to standard treatments like antiemetics, proton pump inhibitors, and steroids. The delayed diagnosis of gastroparesis further complicated management, as its clinical presentation overlapped significantly with hyperemesis gravidarum (HG). Additionally, the presence of subclinical hypothyroidism posed another layer of diagnostic complexity due to its potential exacerbation of symptoms such as nausea and delayed gastric motility.

Treatment

The therapeutic approach for the patient focused on addressing her primary conditions: hyperemesis gravidarum, gastroparesis, and subclinical hypothyroidism, using a combination of pharmacologic and supportive interventions. For hyperthyroidism, the patient was prescribed levothyroxine at a dosage of 100 µg once daily. This medication was taken in the morning on an empty stomach, ideally 30-60 minutes before breakfast, accompanied by a

full glass of water to optimize absorption. Care was taken to avoid the intake of calcium or iron supplements within a 4-hour window of levothyroxine, as these could interfere with its absorption.

To manage the symptoms of gastroparesis and persistent nausea, the patient was prescribed metoclopramide, 10 mg per dose, to be taken three times daily, 30 minutes before meals. This medication promotes gastric emptying and helps reduce nausea and vomiting. However, treatment with metoclopramide was limited to a maximum of 12 weeks due to concerns about the risk of tardive dyskinesia with prolonged use. To address the gastric acid-related symptoms and prevent esophageal and gastric irritation, omeprazole was prescribed at a dosage of 20 mg twice daily, before breakfast and dinner. This proton pump inhibitor was taken to suppress gastric acid production and promote mucosal healing. Additionally, the patient was given sucralfate syrup at a dosage of 15 mL three times daily, to be taken 1 hour before meals and at bedtime. Sucralfate acts by forming a protective barrier in the stomach lining, helping to prevent further irritation and promoting healing of the mucosa. The patient was advised not to take antacids within 30 minutes before or after taking sucralfate, as this could interfere with its action.

Throughout the treatment process, adjustments were made based on the patient's clinical response. As her vomiting subsided and symptoms were managed, the focus shifted toward maintaining adequate hydration and nutrition, both crucial for her health and the health of the fetus. Regular monitoring was conducted to assess the effectiveness of the medications, with further interventions planned as necessary.

Follow-Up and Outcomes

Following the initiation of treatment, the patient experienced significant improvement in her condition. The vomiting subsided, and there was a general improvement in her symptoms after just two days of treatment. This positive response indicated that the combination of levothyroxine, metoclopramide, omeprazole, and sucralfate effectively addressed the primary issues of hyperemesis gravidarum and gastroparesis. Routine follow-up tests were conducted to monitor her progress, including repeat lab tests for thyroid function, electrolytes, and glucose, which showed stable results post-treatment. Imaging and clinical assessments also confirmed the absence of new complications.

Adherence to the prescribed treatment regimen was assessed during follow-up visits, with the patient reporting no significant adverse events, although she was closely monitored for any potential side effects, especially from metoclopramide. Given the nature of the medications, the patient was educated on the importance of timely and consistent medication administration, with particular attention to the timing of levothyroxine and the avoidance of antacids with sucralfate.

In the long term, maternal health shall be closely monitored, particularly regarding mental health, given the psychological toll of prolonged illness during pregnancy. Signs of postpartum depression or anxiety shall be assessed following labor, and appropriate support shall be provided. Nutritional deficiencies shall be evaluated, particularly given the significant weight loss and vomiting the patient experienced in this pregnancy. The patient was advised to maintain ongoing dietary adjustments and medications to manage any possible symptoms of gastroparesis, ensuring both her health and the potential health of future pregnancies.

DISCUSSION

Hyperemesis gravidarum (HG) is a severe form of pregnancy-related nausea and vomiting, distinct from common morning sickness due to its intensity, duration, and associated complications such as weight loss and dehydration.[1] Hormonal changes, particularly elevated levels of human chorionic gonadotropin (hCG), estrogen, and progesterone, play a crucial role in the pathophysiology of HG. Human chorionic gonadotropin, produced by the placenta, is believed to stimulate the vomiting center in the brain. Although essential for maintaining pregnancy, hCG levels peak early in gestation and are thought to be disproportionately elevated in women with HG, triggering more severe symptoms.[5]

Progesterone contributes to HG through its effects on the gastrointestinal tract. By relaxing smooth muscles, including the lower esophageal sphincter, progesterone causes delayed gastric emptying, increased gastric acid secretion, and gastric stasis, which exacerbate nausea and vomiting. Its effects on the autonomic nervous system may further alter gastric motility, contributing to fullness, dehydration, and malnutrition that can complicate pregnancy.[6] HG receptor mechanisms involve interactions between hormones, receptors, and signaling pathways. Estrogen can sensitize the vomiting center in the brainstem via estrogen receptor binding. Neurokinin-1 (NK1) receptor activation by substance P plays a key role in the emetic response. In HG, elevated hormone levels may disrupt neurotransmitter balance, enhancing symptom severity and persistence.[7]

Gastroparesis is characterized by delayed gastric emptying without mechanical obstruction and is an important differential diagnosis in severe nausea and vomiting during pregnancy.[3] Pregnancy-related hormonal changes, particularly elevated progesterone levels, play a significant role in its development. Progesterone induces smooth muscle relaxation throughout the gastrointestinal tract, reducing gastric motility and delaying gastric emptying, while also affecting the lower esophageal sphincter and increasing the risk of gastroesophageal reflux, which can exacerbate nausea and vomiting.[8] Anatomical and physiologic changes during pregnancy further contribute to delayed gastric emptying. As pregnancy progresses, uterine enlargement displaces and compresses the stomach and intestines, slowing gastric transit and worsening symptoms such as fullness, bloating, and postprandial discomfort. These effects are more pronounced in the second and third trimesters, when mechanical impedance of gastrointestinal function is greatest.[2] Rising progesterone levels interact with gastric smooth muscle receptors, including the progesterone receptor, leading to impaired motility. Pregnancy-related

autonomic changes, with increased sympathetic and reduced parasympathetic tone, further inhibit gastric emptying. Although compensatory neurohormonal responses such as increased motilin may occur, elevated progesterone levels and mechanical factors may overwhelm these mechanisms, preventing restoration of normal gastric emptying.[8]

Subclinical hypothyroidism, characterized by elevated TSH with normal FT4, reflects impaired thyroid hormone activity without overt clinical symptoms. Thyroid hormones (T4 and T3) are essential regulators of gastrointestinal motility, particularly during pregnancy. Increased TSH suggests insufficient thyroid hormone action, which can slow gastrointestinal transit. Thyroid hormones act via thyroid hormone receptors (TRs) in gastrointestinal smooth muscle cells to regulate contraction and relaxation necessary for normal peristalsis; reduced hormone activity therefore results in delayed gastric emptying and constipation.[9]

The gastrointestinal effects of hypothyroidism are primarily mediated through altered motility. Thyroid hormones stimulate smooth muscle contraction via TRs and β1- and β2-adrenergic receptor pathways. In subclinical hypothyroidism, reduced thyroid hormone availability decreases β-adrenergic receptor activity, leading to impaired motility. Thyroid hormones also regulate gastrointestinal hormones such as motilin and gastrin, and their imbalance may further exacerbate nausea, bloating, and delayed gastric emptying. Thyroid hormone deficiency additionally affects gastrointestinal function through modulation of the autonomic and enteric nervous systems. Normally, thyroid hormones promote parasympathetic activity and coordinated gut motility. In subclinical hypothyroidism, relative sympathetic predominance and altered enteric neurotransmitter release, including serotonin dysregulation, contribute to reduced motility and prolonged transit time.[9]

Management of hyperemesis gravidarum (HG) focuses on symptom control and prevention of dehydration, electrolyte imbalance, and malnutrition. Pharmacological therapy is central. Metoclopramide acts as both a dopamine D2 receptor antagonist in the chemoreceptor trigger zone and a prokinetic agent in the gastrointestinal tract via serotonin receptors (5-HT3 and 5-HT4). This dual central and peripheral action reduces nausea and vomiting while improving gastric motility and delayed gastric emptying, alleviating bloating and supporting nutrient absorption critical for maternal and fetal health.[5]

Proton pump inhibitors such as omeprazole are commonly added to address acid-related symptoms. By irreversibly inhibiting the H^+/K^+-ATPase in gastric parietal cells, omeprazole reduces gastric acid secretion, which may be increased due to prolonged vomiting. Acid suppression provides relief from reflux symptoms and reduces the risk of esophagitis and ulcer formation, reflecting the molecular basis of acid-mediated mucosal injury in HG. Non-pharmacological measures remain essential. HG carries a substantial psychological burden, and anxiety or stress may exacerbate symptoms via the gut–brain axis and activation of the hypothalamic-pituitary-adrenal axis. Psychological support and dietary modifications, including small frequent meals and avoidance of triggers, can reduce gastric distension and improve gastric emptying, complementing pharmacological therapy.[10]

This case report highlights the diagnostic and management challenges in a pregnant patient with hyperemesis gravidarum (HG), gastroparesis, and subclinical hypothyroidism. HG, characterized by severe nausea and vomiting, poses significant risks to maternal and fetal health, exacerbated by gastroparesis, which delays gastric emptying, and subclinical hypothyroidism, which can worsen gastrointestinal symptoms. Diagnosing these conditions is challenging, especially distinguishing between normal pregnancy changes and pathological symptoms. Effective management involved anti-nausea medications, prokinetic agents, thyroid hormone replacement, and nutritional support. A multidisciplinary approach was essential to prevent complications like dehydration and fetal growth restriction. This case underscores the importance of individualized care and thorough evaluation of thyroid function in pregnant women, while also highlighting the need for further research to explore the complex interplay of gastrointestinal, hormonal, and metabolic factors in pregnancy.

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CONFLICT OF INTEREST

The authors have no conflicts of interest to declare.

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