Endocrine disorder in pregnancy and hyperemesis gravidarum

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Objectives

- *Know the Course of thyrotoxicosis in pregnancy*
- *Know the Course of hypothyroidism in pregnancy*
- *Hyperemesis gravidarum---definition ,clinical features, pathogenesis and management.*

Thyroid disease

- Thyroid disease is common in women of childbearing age. Thyroid disease is the second most common endocrine condition encountered in women of childbearing age after diabetes. Most of these conditions are treatable, and may affect mother and fetus adversely if they are not evaluated and managed appropriately.

- Many of the symptoms of thyroid disease, such as heat intolerance constipation, fatigue, palpitations and weight gain, resemble those of normal pregnancy and therefore new presentations of thyroid disease can be difficult to detect during pregnancy.

- **Physiological changes** of pregnancy, including plasma volume expansion, increased thyroid binding globulin production and relative iodine deficiency, also mean that thyroid hormone reference ranges for non-pregnant women are not useful in pregnancy.

- Free thyroxine 4 (fT4), free T3 (fT3) and thyroid-stimulating hormone (TSH) should be analyzed when assessing thyroid function in pregnancy, and total T3 and T4 not used.

Physiologic Changes in Thyroid Function During Pregnancy

Maternal Status	TSH **Initial screening test**	Free T4	Free Thyroxine Index (FTI)	Total T4	Total T3	Resin Triiodothyronine Uptake (RT3U)
Pregnancy	No change	No change	No change	*Increase*	*Increase*	*Decrease*
Hyperthyroidism	Decrease	Increase	Increase	Increase	Increase or no change	Increase
Hypothyroidism	Increase	Decrease	Decrease	Decrease	Decrease or no change	Decrease

Thyrotoxicosis in PREGNANCY

Causes:

- Graves disease(90%)

which is an autoimmune disorder with high levels of circulating thyroid stimulating antibodies

- Toxic multinodular goiter
- Toxic adenoma
- Thyroid carcinoma
- Subacute thyroiditis
- Biochemical thyroiditis(as in pregnancy-mole)

Gestational hyperthyroidism :

- Gestational hyperthyroidism or gestational thyrotoxicosis is used when there are symptoms of hyperthyroidism due to the high levels of HCG, which causes thyroid hyperfunction. This condition needs to be differentiated from Graves' disease, as most of the symptoms are similar to those in pregnancy. Up to 15% of normal pregnancy TSH can be suppressed due to hCG effect; they do not require extra treatment; careful observation is good enough. There is another entity in pregnancy called transient gestational thyroticosis, where free thyroid hormone can be increased, and they require a short course of anti-thyroid medication. Gestational thyrotoxicosis is usually transient and recovers over a period of few weeks. This is essentially a retrospective diagnosis.

Clinical features in pregnancy

- Weight loss
- Tremor
- Persistent tachycardia
- Eye signs
- Hyperemesis gravidarum

Diagnosis

- Increase free T4,freeT3.
- Decrease TSH.
- Prescence of autoimmune antibodies.

Effect of pregnancy on thyrotoxicosis

- Usually improve in the second and third trimester due to immune suppression .
- Deteriorate in the post partum period

Effect of thyrotoxicosis on pregnancy

Well controlled----no effect on fetus or mother with good outcome

Untreated or poorly controled---cause:

Subfertility

Miscarriage

IUGR

PTL

Stillbirth

Thyroid crisis

heart failure

maternal mortality

fetal goiter

fetal thyrotoxicosis

fetal **hypothyroidism**

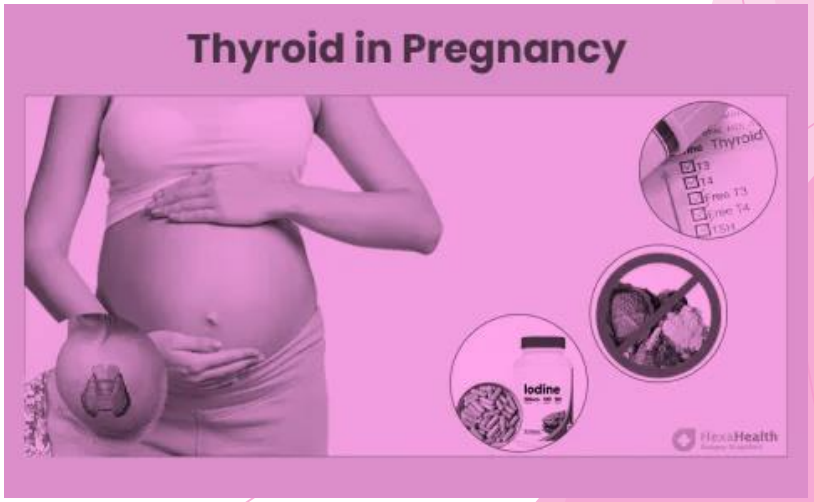
Management

- ANC—endocrinologist should be involved, aiming for euthyroid state as early as possible with the lowest doses of antithyroid drugs
- Serial growth scan ----risk of IUGR
- Fetal echocardiography (20week)
- Treatment of any infection or anemia(to avoid stress that predispose to thyroid storm)

- Antithyroid drugs---PTU, carbimazol(PTU is preferred because it less cross the placenta and less secreted with breast milk)
- B-blocker—Propranolol(used for short term for symptomatic relief
- Surgery--- rarely used ,if needed it is done in the second trimester, and it is indicated if there is retrosternal goiter , no response to treatment, suspected malignancy.
- Radioactive iodine **should not be** used.
- Surgery is rarely indicated.

Hypothyroidism

It affects approximately 1% of pregnant women. Providing thyroxine replacement therapy is adequate, hypothyroidism is not associated with an adverse pregnancy outcome for the mother or fetus



Causes

It is more common

- Hashimoto thyroiditis
- Atrophic thyroiditis
- Iatrogenic(thyroidectomy)

Drugs(antithyroid,lithium,iodine,amiodaron) The commonest cause is iodine deficiency which may result in cretinism of the newborn

Clinical features

- Cold intolerance
- Bradycardia
- Slow tendon reflexes

Diagnoses

- Low freeT4
- increase TSH
- Presence of autoimmune antibodies
- *TSH level is more useful in diagnosis of hypothyroidism in pregnancy*

Effect of hypothyroidism on pregnancy

- Anovulatory infertility
- Miscarriage
- Preeclampsia
- PTL
- Low birth weight, , fetal distress, and impaired neuropsychological development
- Fetal hypothyroidism
- Placental abruption
- The fetus depends on maternal thyroid hormones for normal brain development until 12 week when fetal thyroid start functioning

Post-partum thyroiditis

Post-partum thyroiditis is associated with the presence of thyroid anti peroxidase antibodies. The incidence varies between 2 and 16%. It is characterized by an initial hyperthyroid phase that classically occurs 1–3 months post-partum, followed by a hypothyroid phase, which usually resolves by 12 months after delivery.

The hypothyroidism may require treatment with thyroxin, but treatment should be stopped after 1 year as many cases resolve.

However, there is a risk of developing subsequent hypothyroidism in women who have had post-partum thyroiditis, so affected women should have their thyroid function checked regularly.

Management

- ANC---endocrinologist should be involved
- Asses her TFT(thyroid function test)especially in the first trimester
- Regular fetal scanning
- Levothyroxine is safe during pregnancy
- Iron supplementation and antiacids' containing aluminum hydroxide interfere with thyroxin absorption so they should be taken at different time

Pituitary disorders:

- For **microadenoma** the treatment is usually stopped during pregnancy, it may enlarge during pregnancy but rarely cause a problem, with frequent monitoring of visual field, if tumour enlarges then treatment is recommended.
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- For **macroadenoma** (>1cm size) it is best to continue with dopamine agonist because the risk of tumour enlargement, there is no evidence that drugs are teratogenic.

Cushing syndrome

- Most females are infertile, if get pregnant then high incidence of preterm delivery and still birth.
- The diagnosis is difficult because the symptoms mimic normal pregnancy changes as striae, weight gain, weakness, hypertension and diabetes.
- Assay of plasma cortisol, CT, US, MRI are indicated

Addison disease

- Presents with exhaustion, hypotension, hypoglycemia and wt loss
- Occasionally may present with crisis which is treated with fluid and glucocorticoid
- Treatment: replacement with steroids should continue during pregnancy with parenteral therapy at time of stress such as labour

Phaeochromocytoma:

- Is rare presents with hypertensive crisis like preeclampsia, characteristic feature is paroxysmal hypertension, other features as headache, blurring of vision, anxiety and convulsion.
- Diagnosis: measurement of the level of catecholamines
- Treatment: alpha blockers and phentolamine, preferably delivery by caesarean section to avoid the sudden increase in catecholamines associated with delivery

Hyperemesis Gravidarum

is a severe, intractable form of nausea and vomiting that causes imbalance of fluid and electrolytes, disturbs nutritional intake and metabolism, causes physical and psychological debilitation and is associated with adverse pregnancy outcome, including an increased risk of preterm birth and low birth weight babies

Incidence

- it affects 0.3 – 2 % of pregnancies, the aetiology is unknown and appears to be multifactorial
- Population incidences vary, and there appears to be an ethnic or familial predilection
- It appears to be related **to high or rapidly rising serum levels of pregnancy-related hormones possibly:**
- **human chorionic gonadotropin (hCG) and estrogens**

- There are interrelated **psychologica**l components (more common in anxious women)
- Other factors that increase the risk for admission include hyperthyroidism, previous molar pregnancy,

diabetes, gastrointestinal illnesses, and asthma.

- An association of H. pylori infection has been proposed

pathogenesis

- During pregnancy there is increase in estrogen,progesteron and b-HCG
- All causes relaxation of gastroesophageal sphincter and delay gastric emptying

- Excessive vomiting sever enough to cause dehydration, weight loss ,hypovolemia, electrolyte disturbance, and behavioral disorders in the first trimester and up to 16 week of gestation
- Electrolyte disturbance include-----decrease K,Na and hypochloremic alkalosis
- mean time of onset----5-6 weeks
- Peak at----9weeks
- Subsides---16-20 weeks
- Persistent until third trimester---15-20%

Risk factors

- Family tendency
- Female fetus
- Age>35 year
- Nulliparity
- Previous HG
- Motion sickness
- *Smoking and alcohol are protective factors*

Clinical presentations

- Nausea and vomiting
- Weight loss(5%of pre pregnancy weight)
- Ketonuria
- Orthostatic hypotension
- Physical signs of dehydration (dry and coated tongue, delayed skin turgor, postural changes in blood pressure and pulse

rate) significant weight loss, jaundice,

- metabolic acidosis in sever case
- Ptyalism(excessive salivation in 60%)

Maternal Complications:

- 1. **Vomiting** may be prolonged, frequent, and severe causing Mallory-Weiss tears bleeding, pneumothorax, pneumomediastinum and esophageal rupture.
- 2**. Depression** that could be a cause or an effect.
- 3. **Wernickes encephalopathy**: CNS dysfunction due to deficiency in thiamine B1 presents with apathy, confusion, ataxia and blindness. long-term sequelae are common and include blindness, convulsions and coma. A third of women have an abnormal electroencephalogram (EEG).
- 4. Various degrees of **acute renal failure** from dehydration are encountered that may require dialysis.

5. **Hypoprothrombinemia—vitamin K** deficiency causing maternal coagulopathy and fetal intracranial hemorrhage

6. **Thromboembolism** and hepatic failure
7. **Central pontine mylenolysis**, acute peripheral neuropathy and maternal death

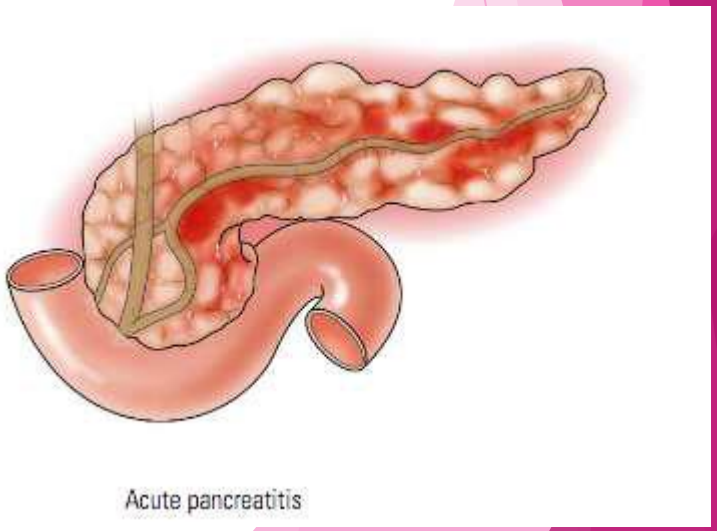
Fetal complication

Outcome is generally good, however if there is maternal weight loss more than 10% then poor
fetal outcome in form **of preterm labour, fetal**
growth restriction and fetal death is expected.

Diffrencial diagnosis

medical:

- Gastroenteritis hepatitis
- Pyelonephritis , UTI
- Pancreatitis hyperthyroidism
- Diabetic ketoacidosis
- Drug induced



Acute pancreatitis

- **Surgical:**
- Appendicitis
- Peptic ulcer
- Cholecystitis
- Intestinal obstruction

- **Gynecological:**
- Red degeneration of a fibroid
- Twisted ovarian cyst
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Obstetrical:

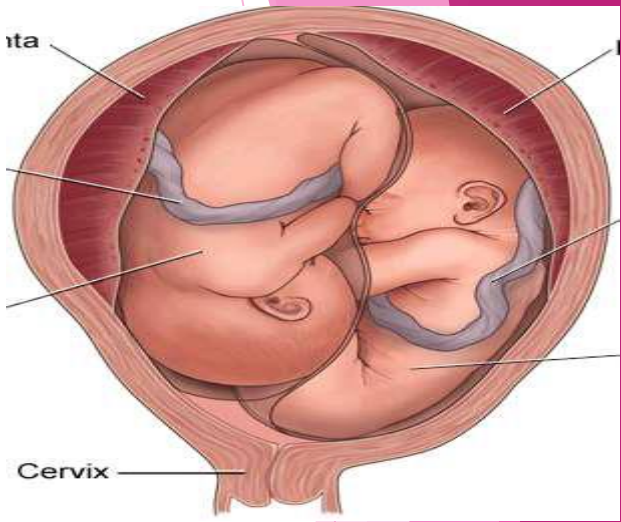
Twin

Molar pregnancy

Sever PET

Acute fatty liver

Down syndrome



Complications

Maternal

- Wernicks encephalopathy----due to vit.B1 deficiency
- Central pontine myelinolysis---due to hyponatremia
- Mallory Weiss syndrome
- Esophageal rupture
- Renal and liver failure
- Maternal death

fetal

- IUGR,PTL,IUD

Diagnosis:

- A pregnant woman presents with excessive nausea and vomiting. The diagnosis of hyperemesis is by exclusion of other causes of nausea and vomiting which could be: **(DDX)**
- Gastrointestinal: peptic ulcer, gastroenteritis, gastro-esophageal reflux and pancreatitis.
- Genitourinary: pyrlonephritis, renal stone and leiomyoma red degeneration.
- Metabolic: diabetic ketoacidosis and hyperthyroidism.
- Neurological: tumours and meningitis
- Others: poisoning, psychological and fatty liver of pregnancy

Investigations

- CBC hemoconcentration(raised PCV)
- GUE---ketone bodies
- Urine culture
- Liver function test
- Ultrasound to confirm pregnancy <exclude molar pregnancy
- Thyroid function test
- RBS
- Electrolytes: decreased Na, K , Cl
- Metabolic alkalosis

Management

- Advice the patient to eat every 2 hours
- Take 6 small meals
- Add ginger to diet
- Avoid triggering items
- **Psychologica**l support and home environment

In sever cases

- **Hospital admission**
- **Nil by mouth** until improvement then start small frequent meals
- **Psychological support**
- **I.V. fluids**---normal saline or Hartman solution normal saline 1 L+ 20-40 mmolKCL 8-hourly. Dextrose

is better to be avoided as it may precipitate Wernicke's

encephalopathy. Continue the fluid until the patient can take oral fluid or no ketones in urine.

- **Daily** sent for renal function test and serum electrolytes

Pharmacologically

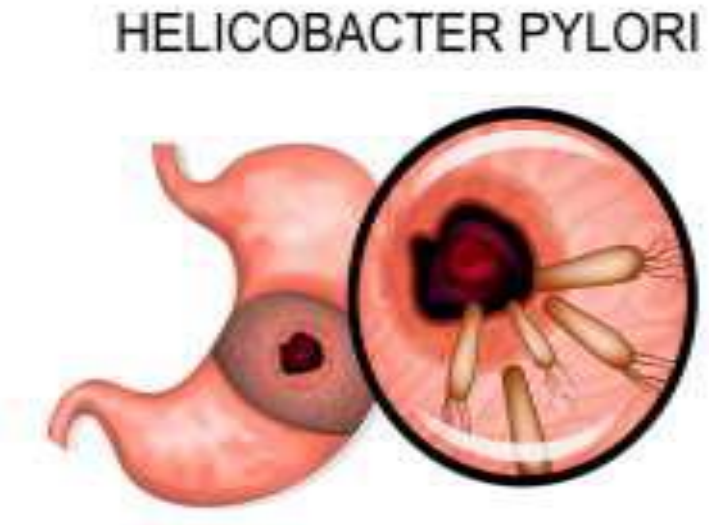
- **Vitamin therapy**: B6 10-30 mg per day is safe and reduces the nausea.Thiamineorally 25-50 mg td or IV 100mg weekly

Antiemetics---therapy: are safe in pregnancy, antiemeticssuch as cyclizine50mg , promethazine 25mg, chlorpromazine 10mg or metoclopramide

Steroids: there is little evidence that treatment with glucocorticosteroidsis effective

- -Parenteral nutrition
- **Termination of pregnancy**

If patient is not responding to pharmacological therapy test for H-pylori




Thank You
Loves Made Me