Maternal physiology during pregnancy

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anatomical changes

- The body of the uterus
  - Height and weight (hyperplasia)
    - the height increases from 7.5 cm to 35cm
    - the weight increases from 50g to 1000g at term
  - Uterine ligaments
    - show hypertrophy
  - Dextro-rotation
    - the uterus is tilted and twisted to the right in 80% of cases
- Lower uterine segment (LUS)
  - the LUS is formed from the isthmus
  - The lower uterine segment (LUS) is the part of the uterus and the upper cervix which lies between the attachment of the peritoneum of the uterovesical pouch superiorly & the internal cervical os inferiorly. The isthmus of the uterus, the lower extremity of which joins with the cervical canal
• The cervix
  - edema and congestion, and becomes soft
  - mucus plug (operculum): cervical mucus closing the cervical canal
  - increased secretion from its glands

• The vulva
  - shows increased vascularity and varicosit
- The vagina
  - shows increased vascularity soft, moist and bluish
  - distention of vagina at birth
- The ovary
  - shows increased vascularity and size
  - one ovary contains the corpus luteum
- Pelvic ligaments
  - relaxation of the ligaments
  - relaxation of the pelvic joints
  - the pelvis become more mobile and increases in capacity
Breast changes

- Increased size and vascularity
  warm, tense and tender
- Increased pigmentation of the
  nipple and areola
- Secondary areola appear (light
  pigmentation around the 1ry
  areola)
- Montgomery tubercules appear
  on the areola (dilated sebaceous
  glands)
- Colostrum like fluid is
  expressed at the end of the 3rd
  month
Skin changes

- Pigmentation due to increased melanocyte stimulating hormone:
  - linea nigra: pigmentation of the linea alba, more marked below
  - the umbilicus
  - chloasma gravidarum: Butterfly pigmentation of the face (mask of pregnancy)

- Striae gravidarum
  - stretch of the abdominal wall rupture of the subcutaneous elastic fibers
  - pink lines in flanks - become white after labor
There is an increase weight of approximately 12.5 Kg at term

- The main increase occurs in the 2nd half of the pregnancy, 0.5Kg/week
- Causes:
  - growth of the conceptus
  - enlargement of the maternal organs
  - maternal storage of fat
  - increase in maternal blood and interstitial fluid
Endocrine changes
human chorionic gonadotrophin (HCG):

- it is secreted by trophoblast and can be detected in serum 10 days after conception.
- there is high level of circulating HCG in early pregnancy (to provide a suitable environment for implantation and development).
- Function to support corpus luteum secretion of estrogen and progesterone in the first trimester until the placenta becomes able to produce these hormone.
- the peak level normally occur in the 12th week.
- normally disappear from urine 7-10 days after delivery of placenta.
Human placental lactogen (HPL)

- It is secreted by syncytiotrophoblast.
- It is level increase when the level of HCG start to drop.
- Has minimal effect on fetus.
- HPL effect on:
  1. The breast:
     - Mammary growth during pregnancy.
     - Production of colostrum.
     - Milk production.
  2. Proteins → HPL stimulates protein synthesis at cellular level.
  3. Carbohydrate:
     - Stimulate insulin secretion.
     - Inhibit insulin action.
  4. Fat → HPL mobilizes fat from body store (lipolysis) lead to increase maternal blood glucose and maternal tissue cannot utilize the glucose so the glucose will be available for fetus.
Estrogen

- produced by corpus luteum in early pregnancy.
- by placenta (estrone and estradiol) and fetal adrenals (estriol) in late pregnancy.
- Levels continue to increase till term
- Estriol accounts for 85%

**Role of estrogen:**
- **On connective tissue:** leads to loose and pliable connective tissue mainly in the cervix.
- **On the protein:** estrogen stimulate directly RNA synthesis lead to protein synthesis.
- **On the uterus:** induces its growth and controls its function.
progesterone

- It is production same as estrogen.
- Levels increases steadily during pregnancy.
- It has effect on smooth muscle leads to muscle relaxation mainly in uterus.
- Accounts for smooth muscle relaxation leading to:
  - Constipation, delayed gastric emptying
  - Reduced bladder and ureteric tone.
  - Venous dilation.
  - Reduced diastolic pressure.
Endocrine changes - thyroid gland

- Production of thyroid hormone increases by 40% to 100% to meet maternal and fetal demands
- The thyroid gland undergoes moderate enlargement during pregnancy
- Circulating thyroid hormone exists in two primary active forms: thyroxine (T4) and triiodothyronine (T3).
- TBG is increased during pregnancy because the high estrogen levels induce increased hepatic synthesis
- the free, biologically active concentration of each hormone is unchanged.
Endocrine changes- thyroid gland

- clinically, the free T4 is an appropriate measure of thyroid function and the main determinants of whether a patient is euthyroid during pregnancy
- TSH levels are decreased slightly in the first trimester (when HCG levels are at their highest). They increase again at the end of the first trimester, and the upper limit in pregnancy is raised to 5.5 μmol/l compared with the level of 4.0 μmol/l in the non-pregnant state.
Endocrine changes- thyroid gland

- Only minimal amounts of thyroid hormone cross the placenta. However, the fetus is reliant on maternal thyroxine to maintain normal fetal thyroid function.
- The production and secretion of fetal thyroid hormone starts at around the 20th week of gestation.
Endocrine changes - pituitary gland

- Serum prolactin levels increase in the first trimester and are 10 times higher at term.
- (FSH) and (LH) levels are almost undetectable during pregnancy.
- Pituitary growth hormone production is decreased but serum growth hormone levels are increased due to growth hormone production from the placenta.
- Oxytocin levels increase in pregnancy and peak at term.
Gastrointestinal tract changes
Gastrointestinal tract

- **Nausea and vomiting:**
  - affect 50-90% of pregnancies.
  - human chorionic gonadotropin (hCG), estrogen, progesterone, and thyroid hormones could all be involved in the etiology.
  - The nausea symptoms usually resolve by week 20 but about 10-20% of the patients experience symptoms beyond week 20 and some until the end of the pregnancy.
  - About 0.5-3% of pregnant women develop hyperemesis gravidum, a severe form of nausea and excessive vomiting, often resulting in dehydration, electrolyte imbalance, ketonuria, weight loss and vitamin or mineral deficiencies.
Gastrointestinal tract

- **Gums:**
  - Becomes hyperemic and soft
  - More prone to bleeding from minor trauma.
- **Increased salivation (ptyalism)**
- **Alteration in sense of taste.**
- **Increased appetite and thirst.**
Gastrointestinal tract

**Heartburn:**
- Reduced tone of the lower esophageal sphincter leading to reduced intraesophageal pressure.
- Esophageal peristalsis has lower amplitude and lower speed.
- Stomach is increasingly displaced upwards by the gravid uterus leading to an altered axis and increased intra-gastric pressure.

**Stomach:**
- Decreased tone and motility (due to the effects of progesterone)
- Decreased gastric acid secretion, increase in gastric mucus
Gastrointestinal tract

**Small bowel:**
- Reduced motility of small bowel
  - increased transit time in the third trimester and postpartum
- Enhanced iron absorption

**Colon:**
- Constipation
  - Mechanical obstruction by the uterus
  - Reduced motility
  - Increased water absorption
Gastrointestinal tract - Liver

- Spider angiomata and palmar erythema develops (elevated estrogen levels)
- **Gallbladder:**
  - Biliary cholesterol saturation increases and chenodeoxycholic acid decreases
    - increased risk gallstone formation
Skeletal and bone density changes

- Exaggerated lordosis of the lower back
- Joint laxity in the anterior and longitudinal ligaments of the lumbar spine
- Widening and increased mobility of the sacroiliac joints and pubic symphysis.

Bone density:
- Although pregnancy and lactation are associated with reversible bone loss, studies do not support an association between parity and osteoporosis in later life.
- Bone turnover is low in the first trimester and increases in the third trimester when fetal calcium needs are increased.
Metabolic changes

- By the third trimester, maternal basal metabolic rate is increased by 10% to 20% compared with that of the non-pregnant state.
Weight Gain in Pregnancy

- The average weight gain in pregnancy uncomplicated by generalized edema is 12.5 kg (28 lb).

- The products of conception constitute only about 40% of the total maternal weight gain.
INSULIN EFFECTS AND GLUCOSE METABOLISM

- Increased insulin secretion, increased insulin sensitivity in early pregnancy, followed by progressive insulin resistance.
- In pregnancy, the insulin response to glucose stimulation is augmented.
- Glycogen synthesis and storage by the liver increases, and gluconeogenesis is inhibited. Thus, during the first half of pregnancy, the anabolic actions of insulin are potentiated.
Insulin levels are increased in both the fasting and postprandial states in pregnancy. Fasting glucose levels are however decreased due to:

- increased storage of tissue glycogen
- increased peripheral glucose use
- decrease in glucose production by the liver
- uptake of glucose by the foetus
If a woman’s endocrine pancreatic function is impaired, and she is unable to overcome the insulin resistance associated with pregnancy then gestational diabetes develops.
INSULIN EFFECTS AND GLUCOSE METABOLISM

To summarize:

Pregnancy is a diabetogenic state and the adaptations in glucose metabolism allow shunting of glucose to the foetus to promote development, while maintaining adequate maternal nutrition.

Normal pregnancy is characterized by mild fasting hypoglycemia, postprandial hyperglycemia and hyperinsulinemia.

The effect of the placental hormones on insulin sensitivity is made evident postpartum when there is a sudden decrease in insulin resistance.
Protein metabolism

- Pregnant women require an increased intake of protein during pregnancy.
- Amino acids are actively transported across the placenta to fulfill the needs of the developing fetus.
- During pregnancy, protein catabolism is decreased as fat stores are used to provide for energy metabolism.
- Positive nitrogen balance throughout pregnancy.
Calcium metabolism

- Increased calcium absorption is associated with an increase in calcium excretion in the urine and these changes begin from 12 weeks.
- During periods of fasting, urinary calcium values are low or normal, confirming that hypercalciuria is the consequence of increased absorption. **Pregnancy is therefore a risk factor for kidney stones.**
Placental Transfer of Nutrients

- The transfer of substances across the placenta occurs by several mechanisms, including **simple diffusion**, **facilitated diffusion**, and **active transport**.
- **Low molecular size and lipid solubility** promote **simple diffusion**.
- Amino acids are actively transported across the placenta, making fetal levels higher than maternal levels.
- Glucose is transported by facilitated diffusion, leading to rapid equilibrium with only a small maternal-fetal gradient.
- **Glucose is the main energy substrate of the fetus.**
Hematological changes
Hematological changes - Blood volume

- Increases progressively from 6 to 8 weeks’ gestation
- maximum volume at 32-34 weeks → 45% increase

- Results from:
  - estrogen stimulation of renin-angiotensin-aldosterone system.
  - Increase in plasma and erythrocytes volume.
Hematological changes - RBC mass

- Red blood cell mass increases by (20-30% increase) by term
- Moderate erythroid hyperplasia in the bone marrow is present
- Reticulocyte count is elevated.
- Result mostly from elevated plasma erythropoietin levels.
- Production of erythrocyte peaks during the third trimester
Hematological changes - body water

- TBW increases up to (6.5L - 8.5L)
  - At term water content of fetus, placenta and amniotic fluid is 3.5L
  - Another 3L accumulates from increased blood volume, plasma volume, RBC, extravascular and intracellular.
  - Also caused by decreased plasma osmolality of approximately 10 mOsm/kg:
    - Water retention exceeds Na retention.
    - Resetting of osmotic thresholds for thirst and vasopressin

- Pregnancy is a condition of chronic volume overload
FIGURE 4-6 Changes in total blood volume and its components (plasma and red cell volumes) during pregnancy and postpartum. (Redrawn from Peck, 1979, with permission.)
Hematologic changes

Because the augmentation in plasma volumes is higher than that of RBC mass, hemoglobin and hematocrit concentration decreases, mainly due to dilutional effect.

**physiologic anemia of pregnancy**
- may function to decrease blood viscosity
- may improve intervillous perfusion?

However, any hemoglobin level below 11 mg/dl during pregnancy should be considered abnormal, and is mainly due to iron deficiency rather than hypervolemia.
Hematological changes - leukocytes

- Peripheral WBC count rises progressively during pregnancy
  - 1st trimester - mean 9500/mm³ (3000-15,000)
  - 2nd and 3rd trimester - mean 10,500 (6000-16,000)
  - Labor - may rise up to 25,000

- These changes may account for the improvement of some autoimmune diseases during pregnancy.
Hematological changes-platelets and coagulation factors.

- Platelets experience a progressive decline but should remain within normal range (minimal value of 100,000-150,000)
  - Likely due to increased destruction.
  - Partially due to dilutional effect.

- Coagulation factors
  - Increased levels of (Fibrinogen (Factor I), Factors VII through X)
  - No change in prothrombin (Factor II), Factors V and XII
  - Decline in platelet count, Factors XI and XIII and protein S levels
  - Increase resistance to protein C
Hematological changes-platelets and coagulation factors.

- During pregnancy, fibrinogen levels increases by 50%, levels ranges between 300-600 mg/dl.
- This leads to the increased levels of ESR during pregnancy.
- Bleeding time and clotting time are unchanged in normal pregnancy.
- Pregnancy is a hypercoagulable state, leading to increased risk of thromboembolic events.
- Risk is highest during the postpartum period.
Immunology of pregnancy

- In the intervening years, it has become apparent that both the mother and her fetus are immunologically aware of each other, and yet tolerance exists for the most part.

- Pregnancy does not result in an overall maternal immunosuppression.
Immunology of pregnancy

- The placenta, decidua, and the membranes provide the key barrier in protecting the growing fetus from microbial pathogens and toxins circulating in the mother’s blood.
Cardiac Output

- CO = SV * HR
- CO ↑ mainly due to:
  - Early in pregnancy → ↑ in SV
  - Late in pregnancy → ↑ in HR

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<th>First trimester</th>
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<th>Third trimester</th>
<th>Early postpartum</th>
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<td>Heart rate</td>
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Exercise in pregnancy:
O2 consumption, CO are increased to any given amount of exercise compared to non-pregnant state → less cardiac reserve for exercise in pregnancy → less exercise tolerance.
Compression by gravid uterus:
on IVC it causes:
1) Supine Hypotension Syndrome
2) ↑ in pelvic and L.L. venous pressure →
   a. varicose veins in L.L. and vulva
   b. hemorrhoids
   c. edema of pregnancy (contributed also by delutional hypo-albuminemia).
   d. ↑ risk of thrombosis (Ex.: DVT) by blood stasis.
Respiratory effect

- Elevated diaphragm position $\rightarrow$ ↓ negative intra-thoracic pressure $\rightarrow$ ↓ Resting lung volumes (RV, and FRC [ due to lowered RV and ERV; FRC=RV+ERV])
- This will NOT impair diaphragmatic or thoracic muscle movement $\rightarrow$ NO change in Vital capacity
- Minute ventilation= RR*TV $\rightarrow$ RR does NOT change, TV increase by 40% at term.
Cardio-respiratory compensation:
↑ CO and alveolar ventilation, this rise is greater than required to meet the rise in oxygen demand → arterio-venous oxygen difference and PCO2 FALL despite ↑ in O2 consumption.

Dyspnea of Pregnancy
Appears in 60-70% of pregnant women → mechanism is unknown but could be possibly due to ↑ sensitivity of central respiratory chemoreceptor to PCO2 (Progesterone Effect).
Renal Blood Flow and GFR

- ↓
- resistance of both afferent and efferent renal arterioles due to effects of:
  1) Relaxin 2) Endothelin 3) NO

** Careful attention to small fluctuations in serum creatinine is required to detect renal injury in pregnancy.
Serial Blood Pressures before, during and after pregnancy

*P <0.05 versus previous value
Total body oxygen consumption increases about 15% to 20% in pregnancy:

1) uterus and its contents.
2) ↑ maternal renal and cardiac work.
3) ↑ breast tissue mass and ↑ work of the respiratory muscles.
Thank you