

Adrenal diseases in pregnancy

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Endocrine changes during pregnancy

- considerable endocrine changes
- the fetoplacental unit, accounts for a variety of these changes

Estrogen production during pregnancy

- Large quantities of estrogen are produced
- after the first 3-4 weeks of gestation, the placenta produces nearly all of the estrogen.
- The major precursor for estrogen production is dehydroepiandrosterone sulfate, which is synthesized in the fetal adrenal glands

Steroid circulation in pregnancy

- More than 90% of the estradiol and estriol and 85% or more of the progesterone formed in the trophoblast are secreted into the maternal compartment.
- The net transfer of steroids to maternal blood is approximately 10 times that of the net transfer to fetal blood

Fetal adrenals

- adrenals of the human fetus at term are as large as those of adults, weighing 8-10g or more
- Consist by 85% of an inner zone
- fetal adrenals near term, secrete 100-200mg of the estrogen precursor daily.
- The total daily steroid production by the adrenals in an unstressed adult is only approximately 35mg daily

Fetal adrenals

- provide precursors for placental estrogen formation,
- participate in the events that lead to the initiation of labor and to maturation of the fetal lungs.
- a trophic role has been proposed for other hormones, including growth hormone, human chorionic gonadotropin, prolactin, and human placental lactogen

Steroid circulation in pregnancy (2)

- a small amount of cortisol in maternal plasma crosses the placenta, both because the reentry pathway dominates and because cortisol within the trophoblast is converted to cortisone by 11beta-hydroxysteroid dehydrogenase

Steroid circulation in pregnancy (3)

- dehydroepiandrosterone sulfate, dehydroepiandrosterone, androstenedione, and testosterone, do not reach the fetal compartment
- presence of aromatase enzymes of the syncytiotrophoblast that are used for the conversion of C-19 steroids to estrogens.
- protects the female fetus from possible virilization in women who develop androgen-secreting tumors of the ovary during pregnancy

Steroid circulation in pregnancy (4)

- estrogen and progesterone, appears to be formed or secreted by the placenta.
- No evidence indicates that the placenta synthesizes glucocorticoids or mineralocorticoids

Cortisol-ACTH-CBG

- The levels of cortisol in maternal plasma are markedly increased in association with the rise in estrogen production, partly because of a 3- to 4-fold increase in the level of corticosteroid-binding globulin.
- The rate of secretion of cortisol by maternal adrenals is not increased in pregnancy, but the rate of clearance is decreased.
- The corticotropin level is suppressed
- The lowest level of corticotropin is observed early in pregnancy, rising to a maximum between week 26 and term

Renin-Angiotensinogen

- a 4-fold increase in plasma renin activity is evident by the eighth week of gestation.
- Estrogen stimulates the hepatic synthesis of angiotensinogen.
- Estrogen and progesterone, alone or together, stimulate the secretion of renin, which catalyzes the conversion of angiotensinogen to angiotensin I.

Aldosterone

- aldosterone secretion increases during pregnancy.
- Progesterone, levels of which are markedly increased in pregnancy, is a competitive inhibitor of aldosterone in the distal tubule. Therefore, the physiologic effects of increased aldosterone are attenuated in pregnancy.

Addison's dis in Pregnancy

- Before glucocorticoid replacement therapy pregnancy in patients with adrenal insufficiency was associated with a maternal mortality rate of 35-45%.
- In patients with treated autoimmune Addison disease, conception, fetal development, and delivery should not be problematic.

Addison's dis in Pregnancy

- The usual glucocorticoid and mineralocorticoid replacement dosages are continued throughout pregnancy.
- Some patients may require slightly more glucocorticoid in the third trimester

Addison's dis in Pregnancy

- During labor, adequate saline hydration and 25mg of intravenous (IV) cortisol should be administered every 6 hours
- At the time of delivery or if the labor is prolonged, high-dose parenteral hydrocortisone should be administered (100mg q6h or as a continuous infusion)
- After delivery, the dosage can be quickly tapered to a maintenance dose in 3 days.

Addison's dis in Pregnancy

- Occasionally, patients develop severe nausea and vomiting in the first trimester and may need intramuscular (IM) dexamethasone at a slightly increased dose (1mg daily).

Addison's dis in Pregnancy and IUGR

- Maternal cortisol deficiency has been suggested as a possible cause of fetal intrauterine growth restriction.
- Clinical suspicion if fetal growth restriction is associated with abnormally low maternal blood pressure and an unusual increase in skin pigmentation

New onset Addison dis in pregnancy

- is rare in pregnancy,
- but it may present with prolonged vomiting and weight loss.
- adrenal failure should also be added in the differential diagnosis of hyperemesis gravidarum.

Secondary adrenocortical insufficiency

- may occur as a result of hypothalamic or pituitary diseases.
- Primary lymphocytic hypophysitis usually manifests in pregnancy and is associated with pituitary enlargement

Cushings sy. in pregnancy

- slightly over 100 cases of Cushing syndrome in pregnancy have been reported in the literature
- difficult to detect clinically because of the central weight gain, abdominal striae, increased blood pressure, and glucose intolerance associated with normal pregnancy.

Cushings sy. in pregnancy

- Several cases of exacerbation of Cushing syndrome reported.
- In most cases in pregnancy, an adrenal adenoma benign tumor, was the cause of the Cushing syndrome
- Malignant adrenal tumors are rarely observed in association with pregnancy
- in women who are not pregnant pituitary-dependent disease predominates

Cushings sy in pregnancy-diagnosis

- In normal pregnancy morning cortisol levels (mean plus or minus the standard error of mean) of 14.9 ± 4 mg/dL at 11 weeks' gestation and 35.2 ± 10 mg/dL at 26 weeks' gestation; the levels remained elevated until labor and delivery
- Cortisol levels overlap those found in patients with Cushing syndrome;

Cushings sy in pregnancy-diagnosis

- simple overnight low-dose dexamethasone suppression test are inaccurate in the presence of excess estrogen and in pregnancy.
- Random measurement of urinary or plasma cortisol is not helpful

Cushings sy in pregnancy-diagnosis

- midnight cortisol level can still be very helpful in making the diagnosis
- Normal pregnancy demonstrates 50% suppression of the midnight cortisol level compared with the morning cortisol level
- The standard protocols for low-dose (2mg) and high-dose (8mg) dexamethasone tests have been used safely, and interpretation of suppression of 24-hour urine cortisol and plasma cortisol levels seems to yield reliable results

Cushing's syndrome in pregnancy-diagnosis corticotropin levels

- corticotropin levels are not useful in distinguishing between pituitary and adrenal etiologies
- For all forms of Cushing syndrome in pregnancy, corticotropin levels are normal
- or they are high secondary to placental corticotropin production or owing to placental corticotropin-releasing hormone–stimulated pituitary corticotropin production

Cushings sy in pregnancy-diagnosis

- If the corticotropin level is clearly elevated, a pituitary cause must be considered.
- Ultrasonography or magnetic resonance imaging (MRI) may be used to limit radiation exposure to the fetus

Cushing sy risks in pregnancy

- Hypertension becomes worse in two thirds of patients
- [Preeclampsia](#) or pregnancy-induced hypertension is noted in approximately 10% of patients.
- [Gestational diabetes mellitus](#) occurs in approximately one third.
- Congestive heart failure associated with severe hypertension occurs in 10%.

Cushing sy risks in pregnancy

- Severe proximal myopathy
- mental problems ranging from emotional lability
- psychosis
- Wound breakdown after surgery: vaginal delivery is preferable to cesarean delivery in patients with Cushing syndrome

Cushing's risks in pregnancy

- Premature delivery occurs in two thirds of cases.
- The overall perinatal mortality rate is 15% of reported cases; half were stillborn

Cushing sy risks in pregnancy- cortisol withdrawal problems

- mother may develop cortisol deficiency after a successful [adrenalectomy](#)
- neonate may have cortisol deficiency soon after birth

Treatment of Cushing sy. in pregnancy:

Adrenalectomy

- surgical treatment during pregnancy is safe and significantly reduces fetal losses, premature labor, and maternal morbidity
- The ideal timing for adrenalectomy- retroperitoneal laparoscopic adrenalectomy is early in the second trimester
- After adrenalectomy: Immediately on cortisol replacement,
- continue until the hypothalamic-pituitary-adrenal axis returns to normal.
- Replacement treatment could take several months
- weaning from replacement doses should not be attempted until after delivery

Cushing sy in pregnancy: ketoconazole

- [Ketoconazole](#) has been used successfully in 3 patients during pregnancy. One patient had pituitary-dependent Cushing disease.
- Pregnancy and vaginal delivery at 37 weeks' gestation passed uneventfully,
- newborn male infant did not show any congenital malformation and had normal sexual development

adrenal carcinomas in pregnancy

- termination of the pregnancy may be considered so that definitive therapy can be undertaken
- is a rare and severe disease
- associated with poor fetal and maternal outcome

Primary hyperaldosteronism in pregnancy

- rare cause of hypertension in pregnancy
- Hypokalemia should be corrected before making a biochemical diagnosis because a low potassium level suppresses aldosterone
- Avoid diuretics, ca-channel blockers and beta blockers to make a diagnosis

Diagnosis of primary hyperaldosteronism in pregnancy

- Normally plasma aldosterone levels rise in pregnancy to the primary hyperaldosteronism range
- In a healthy pregnancy, plasma renin activity is usually increased, but it decreases in the setting of primary hyperaldosteronism.

Primary hyperaldosteronism diagnosis in pregnancy

- dynamic test that may be used is stimulation of renin production by positioning the patient in an upright posture
- In pregnant patients, prolonged upright posture results in a modest increase in plasma renin activity.
- If the renin activity remains suppressed, this is suggestive of primary hyperaldosteronism

Primary hyperaldosteronism diagnosis in pregnancy

- Ultrasonography
- MRI

Treatment of primary hyperaldosteronism in pregnancy

- If an adrenal adenoma is detected, unilateral adrenalectomy is the treatment of choice
- Aim adrenalectomy during second trimester

Treatment of primary hyperaldosteronism in pregnancy

- goals of medical therapy: adequate control of blood pressure and replacement of potassium
- spironolactone and angiotensin-converting enzyme (ACE) inhibitors, are contraindicated in patients who are pregnant
- [Methyldopa](#), beta blockers, and calcium channel blockers have been used with variable outcomes.

Pheochromocytoma in pregnancy

- potentially disastrous for the mother and fetus.
- The main sign of the disease is [hypertension](#)
- overall maternal and fetal mortality rates decreased to 17% and 26%, respectively

Pheochromocytoma presentation in pregnancy

- symptomatic hypertension that is often severe and fluctuating
- associated headache, perspiration, palpitation, and tachycardia
- Although hypertension is the hallmark for pheochromocytoma, it may not be present in all cases

Pheochromocytoma presentation in pregnancy

- arrhythmias,
- postural hypotension,
- chest or abdominal pain,
- visual disturbance,
- convulsions,
- sudden collapse

Screening of pheos in pregnancy

- All pregnant women with:
 1. hypertension associated with headache,
 2. palpitation, or excessive sweating
 3. with a family history of pheochromocytoma or associated syndromes

Diagnosis of pheo in pregnancy

- No alteration in catecholamine metabolism develops specifically because of the pregnant state
- accurate 24-hour urine collections for catecholamine assay with epinephrine and norepinephrine and their metabolites
- Magnetic resonance imaging (MRI) and ultrasonography

Treatment of pheos in pregnancy

- Beta blockade (propranolol) should not be used without prior alpha blockade (phenoxybenzamine), because unopposed alpha-adrenergic activity may lead to vasoconstriction and a hypertensive crisis
- Combined alpha and beta blockade is safe in pregnancy

Treatment of pheos in pregnancy

- Surgical intervention should be performed before 24 weeks' gestation, after adequate alpha blockade has been achieved
- After 24th week treated with alpha and beta blockade from the beginning of the second trimester to term, with good fetal outcomes

Delivery in pregnancies with pheos

- Delivery with adequate alpha blockade
- elective cesarean delivery may be performed, followed immediately by adrenal exploration
- higher maternal mortality rates with vaginal delivery (31%) than with cesarean delivery (19%)