



Human Pregnancy Physiology and Diseases: A Mini Review

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ABSTRACT

Pregnancy causes significant changes in the hypothalamic-pituitary-adrenal axis and adrenal gland function. Some of these changes have clinical features that are similar to adrenal gland disorders. While adrenal disorders are uncommon in pregnant women, they have the potential to cause significant morbidity if they go undiagnosed and untreated. Because the majority of patients with adrenal disorders present with clinical features consistent with normal pregnancy, diagnosis during pregnancy is not uncommon. These disorders require a high level of suspicion because they can have serious obstetrical consequences. This review will go over the normal function of the adrenal glands during pregnancy as well as the role of adrenal hormones during pregnancy.

We will discuss the most common adrenal disorders that occur during pregnancy and review the literature on treatment options. Pregnancy causes significant changes in the hypothalamic-pituitary-adrenal axis and adrenal gland function. Some of these changes have clinical characteristics similar to adrenal gland disorders.

Keywords: Pregnancy; Diagnosis

INTRODUCTION

While adrenal disorders are uncommon in pregnant women, they have the potential to cause significant morbidity if they go undiagnosed and untreated. Because the majority of patients with adrenal disorders present with clinical features consistent with normal pregnancy, diagnosis during pregnancy is not uncommon. These disorders require a high level of suspicion because they can have serious obstetrical consequences.

Pregnancy causes significant changes in several endocrine systems, particularly the hypothalamic-pituitary-adrenal axis and the renin-angiotensin-aldosterone system.

Adrenal gland dysfunction is uncommon during pregnancy. Nonetheless, adrenal deficiencies and excesses can cause significant foetal and maternal morbidity [1]. Diagnosis is difficult because clinical features are similar to normal pregnancy characteristics, and the fetal-placental unit alters maternal endocrine metabolism and feedback. As a result, a high index of suspicion and prompt diagnosis are critical.

DESCRIPTION

Pregnancy alterations

The anterior pituitary gland secretes adrenocorticotrophic hormone (ACTH) in response to the hypothalamic-releasing factor corticotropin-releasing hormone (CRH), which stimulates the release of adrenal glucocorticoids. ACTH secretion varies significantly throughout the day, with an early morning peak and a late evening nadir. ACTH secretion, like the other pituitary hormones, is negatively regulated by feedback from the end product hormone secreted by the adrenals - cortisol. Pregnancy increases the demand for steroid production to meet the increased maternal production of oestrogen and cortisol, as well as the foetal demand for somatic and reproductive growth development. During pregnancy, there are significant changes in adrenocortical function, resulting in increased serum levels of ACTH, cortisol, aldosterone, deoxycorticosterone, and corticosteroid-binding globulin (CBG), resulting in a state of physiologic hypercortisolism [2].

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During pregnancy, most binding globulins increase due to increased hepatic production stimulated by increased oestrogen levels; similarly, CBG nearly doubles. As a result, total plasma cortisol levels rise. Total cortisol levels are nearly threefold normal at the end of pregnancy, simulating a state similar to Cushing syndrome. The increased production of CBG does not account for the higher levels of free cortisol observed during pregnancy. The only metabolically active cortisol compound is free cortisol, which is the fraction of cortisol that is not bound to CBG. Increased urinary free cortisol concentrations and salivary cortisol concentrations indicate a rise in free cortisol, which can be measured using the free cortisol index. Though CRH is primarily secreted by the hypothalamus, increased CRH serum levels during pregnancy are largely due to production by placental and foetal membranes, which secrete CRH into the maternal circulation. This increase in CRH is what causes the elevated cortisol levels seen during pregnancy. After the second trimester, CRH rises exponentially, owing primarily to placental production [3]. CRH and ACTH levels in the blood continue to raise in the third trimester, despite increased total and free cortisol levels. While this is consistent with the primary function of placental CRH secretion. Cortisol hypercortisolism during pregnancy manifests clinically as maternal tiredness, weight gain, hyperglycemia, edoema, and emotional upset. Cushing syndrome during pregnancy is difficult to diagnose because these are normal characteristics of pregnant women.

Deoxycorticosterone (DOC), which is similar to aldosterone and has a strong mineralocorticoid effect, is another important adrenal product. From the first trimester, there is a significant increase in serum DOC. Unlike in the non-pregnant state, plasma DOC does not respond to external manipulations such as increased salt intake, dexamethasone suppression, and ACTH stimulation in late pregnancy.

Other hormonal changes associated with pregnancy include a slight increase in testosterone due to increased sex hormone binding protein synthesis by the liver, a slight increase in androstenedione due to increased adrenal synthesis, and a decrease in dehydroepiandrosterone sulphate levels due to increased renal clearance of the hormone. In addition to these changes, there are up to sevenfold increase in aldosterone, angiotensin II, and plasma renin activity during pregnancy. This renin-angiotensin system upregulation increases sodium retention and plasma volume, primarily due to high circulating aldosterone levels, and maintains normal blood pressure in the setting of gestational vasodilation. A specific phenomenon that can occur during pregnancy is the dissociation of renin and aldosterone levels, such that aldosterone levels are higher than expected in relation to renin levels when compared to the non-pregnant state; this is achieved by the adrenal gland's high responsiveness to angiotensin II.

Cushing syndrome

Cushing syndrome in pregnancy is extremely rare and rarely reported. Only about 150 cases have been described; the majority of them were pituitary and adrenal adenomas, with about 10% being cases of adrenal carcinoma. The occurrence of an ectopic ACTH secretion is extremely rare and has received little attention. As previously stated, the diagnosis of Cushing syndrome during pregnancy is difficult due to

the clinical similarities between the two states [4]. When proximal myopathy and bone fractures occur, clinical suspicion should be raised. Consistent with the clinical similarities to normal pregnancy, non-distinctive laboratory findings add to the difficulty of distinguishing between the conditions. Magnetic resonance imaging without contrast of the pituitary is questionable for Cushing diagnosis during pregnancy, and an ultrasound scan of the adrenals may identify a significant proportion of incidental findings known as "incidentalomas." Other evaluation modalities, such as petrosal venous sinus sampling and CRH stimulation testing, have received little attention.

As a result, when treatment began at an estimated gestational age of 20 weeks, the live birth rate increased from 76% to 89%. The main issue is the acceptability of treatment while pregnant. Ketoconazole is not recommended because it has been linked to intrauterine growth retardation and liver toxicity. Metyrapone's efficacy in pregnancy is questionable, and mitotane should be avoided due to foetal toxicity. Mifepristone, a common obstetric and gynaecological medication, should also be avoided because it interferes with progesterone bioactivity [5].

Inadequate adrenal function

Autoimmune adrenalitis is the most common cause of adrenal insufficiency in the Western world. Infectious causes (e.g., tuberculosis, fungi), metastatic spread of neoplasm, and vascular accidents are less common etiologies. Pituitary neoplasms or pituitary suppression can also cause secondary adrenal insufficiency. Many of the clinical features of adrenal insufficiency, such as weakness, vomiting, hyponatremia, syncope, and hyperpigmentation, are also seen in normal pregnancy. Weight loss, extreme hyponatremia, hypoglycemia, and salt craving are all clinical signs of adrenal insufficiency. Because the placenta and foetus control their own steroid environment, maternal adrenal insufficiency has little effect on foetus development.

Prior to surgery, pheochromocytoma is treated with both alpha- and beta-adrenergic blockade. Blood pressure and heart rate should be stabilized for 14 days prior to surgery; alpha blockers (doxazosin/prazosin) are recommended for 5-7 days, followed by beta blockers (propranolol). The surgical approach is determined by gestational age and the gravid uterus; in early pregnancy, a laparoscopic approach is recommended, whereas in late gestation, an open laparotomy may provide better exposure. Before complete surgical resolution, the mode of delivery is debatable, as both vaginal and caesarean delivery has been described with comparable outcomes.

Major Hyperaldosteronism

Primary hyperaldosteronism (PA), an adrenal gland oversecretion of aldosterone, is currently the leading cause of secondary hypertension. While it is estimated that 0.6-0.8% of pregnant women have PA, the literature is limited. The physiological changes of the renin angiotensin system during pregnancy, as with other adrenal disorders, make diagnosing PA during pregnancy difficult [6]. This is complicated further by the development of gestational hypertension in up to 10% of pregnant women. High aldosterone levels are not diagnostic;

however, low renin concentrations may point to PA, and the aldosterone-renin ratio may help in determining the diagnosis. Because progesterone is a competitive inhibitor of aldosterone in the kidney's distal convoluted tubule.

Hypokalemia associated with hypertension, very high levels of aldosterone and low levels of renin, and an adrenal nodule on imaging may also aid in the diagnosis. The course of PA during pregnancy ranges from clinical improvement to deterioration; data to support counselling are limited. Progesterone's antimineralocorticoid effect may have contributed to the clinical improvement observed, restoring renin and potassium levels and blood pressure to normal levels.

Adrenal hyperplasia

Reduced enzymatic activity at various stages of adrenal steroid biosynthesis results in decreased cortisol production and, in many cases, decreased aldosterone production. Compensatory increases in CRH and ACTH occur, as does an increase in the production of steroid precursors that are not metabolised by the affected enzyme. More than 95% of cases are caused by 21-hydroxylase deficiency caused by CYP21A2 gene mutations; the remaining cases are mostly caused by 11-beta hydroxylase deficiency [7]. The role of prenatal dexamethasone, a therapy that prevents virilization of the affected female infant's external genitalia, is well established. If the foetus is a female, dexamethasone should be given until the baby is born. Dexamethasone should be stopped if this is the case.

CONCLUSION

Adrenal disorders are difficult to diagnose during pregnancy.

A thorough diagnostic approach to these disorders, including laboratory testing, must be tailored to pregnancy. There are no current guidelines for managing these patients; instead, recommendations are based on experience and small case series. Although these have been useful in the diagnosis and treatment of these disorders, more research is needed.

CONFLICT OF INTEREST

The author has no conflicts of interest to declare.

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