Clinics of Oncology

Case Report ISSN: 2640-1037 | Volume 8

Challenges and Advances in the Diagnosis and Treatment of Cushing's Syndrome in Pregnancy

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Received: 12 Aug 2024
Accepted: 20 Sep 2024
Published: 26 Sep 2024
J Short Name: COO

Keywords:

Adrenal adenomas; Cushing's disease; Cushing's syndrome during pregnancy; Corticosteroid-binding globulin; Hypothalamic-pituitary-adrenal axis

Citation:

Huiwen Tan, Zhenmei An, Challenges and Advances in the Diagnosis and Treatment of Cushing's Syndrome in Pregnancy. Clin Onco. 2024; 8(1): 1-9

1. Abstract

Cushing's syndrome (CS) during pregnancy is a rare condition, with fewer than 260 cases reported to date. Adrenal adenomas are the most frequent cause, followed by Cushing's disease (caused by pituitary adenomas). Pregnancy has a significant effect on the maternal hypothalamic-pituitary-adrenal axis, leading to increased hepatic production of corticosteroid-binding globulin (CBG), elevated levels of serum, salivary, and urinary free cortisol, lack of cortisol suppression following dexamethasone administration, and placental production of corticotropin-releasing hormone (CRH) and ACTH. These unique physiological changes during pregnancy complicate the diagnosis of CS, often leading to misdiagnosis, as its symptoms can resemble those of preeclampsia or gestational diabetes. Given the serious maternal and fetal complications associated with CS during pregnancy, prompt diagnosis and treatment are essential. Surgery is generally the preferred treatment, except potentially in the late third trimester, where medical therapy might be considered as a secondary option. Despite the importance of timely diagnosis and treatment, there is no consensus on the optimal approach. This review highlights recent advancements in diagnosing and managing Cushing's syndrome during pregnancy, providing critical insights for clinicians handling this challenging condition in pregnant patients.

2. Introduction

Cushing's syndrome (CS), also referred to as hypercortisolism, can interfere with normal follicular development, prevent ovulation, and result in infertility. It is triggered by excessive secretion of glucocorticoids, particularly cortisol, from the adrenal cortex, due to various underlying causes [1, 2]. The severity of CS can differ widely, and its clinical presentation is diverse. Common symptoms include central obesity, a rounded "moon" face, a fat deposit between the shoulders known as a buffalo hump, facial redness (plethora), excessive hair growth (hirsutism), acne, purple stretch marks (striae), easy bruising, high blood pressure, secondary diabetes, and osteoporosis. However, in atypical or subclinical cases, the condition may only be indicated by abnormal laboratory test results, with no apparent symptoms or physical signs [3]. Cushing's syndrome (CS) is more commonly observed in females, with a male-to-female ratio of 1:3, and it is most frequently diagnosed in individuals between the ages of 20 and 40 [4]. The elevated lev-

els of cortisol in CS not only directly affect ovarian function in females but also have a suppressive effect on the hypothalamic-pituitary-adrenal (HPA) axis [5]. This leads to significant inhibitory effects on the reproductive axis, as corticotropin-releasing hormone (CRH) and CRH-induced pro-opiomelanocortin peptides suppress the secretion of gonadotropin-releasing hormone (GnRH) from the hypothalamus. Furthermore, glucocorticoids inhibit the secretion of luteinizing hormone (LH) from the pituitary gland, as well as estrogen and progesterone production, making estrogen-sensitive tissues, such as the endometrium, less responsive to gonadal steroids [5-7]. This dysfunction leads to decreased, irregular, or absent menstruation and frequently results in infertility [8]. As a result, the occurrence of pregnancy in conjunction with Cushing's syndrome is extremely rare, with an incidence of 0.7-2.4 cases per million population per year. Since the first confirmed case of Cushing's syndrome during pregnancy was reported by Hunt and McConahey in 1953 [9], there have been just over 260 documented cases [10]. Despite significant advancements in the diagnosis and treatment of CS, timely and accurate diagnosis remains challenging for clinicians [11-13]. The physiological hypercortisolism often observed in pregnant women can cause plasma and urinary-free cortisol levels to rise to 2-3 times the upper limit of normal [2, 3]. Moreover, physiological changes in pregnancy, such as weight gain and abdominal striae, can obscure the symptoms of CS, increasing the risk of misdiagnosis or missed diagnosis [2, 14, 15]. Pregnancy complicated by CS is associated with a range of complications for both the mother and fetus [2, 15-18]. Elevated cortisol levels in CS can lead to maternal complications such as hypertension, preeclampsia, diabetes, heart failure, and even death [19]. Fetal complications include preterm birth, growth restriction, adrenal insufficiency, and intrauterine death [8, 20]. The diagnosis and treatment of CS during pregnancy are particularly challenging, and unfortunately, there is still no consensus on the optimal approach. This review explores recent progress in the diagnosis and treatment of CS in pregnancy, offering valuable reference information for clinicians managing this complex condition.

3. Etiology and Pathogenesis of CS in Pregnancy

The etiological distribution of Cushing's syndrome (CS) during pregnancy differs markedly from that in non-pregnant populations. A summary of 136 reported cases of CS in pregnancy by Lindsay et al. [20], in 2005 revealed that adrenal adenomas were the leading cause, accounting for 46% (56 cases), followed by Cushing's disease (pituitary adenomas) at 33% (40 cases), adrenal carcinomas at 10% (12 cases), and other causes such as Carney's complex, pheochromocytoma, ACTH-independent hyperplasia (AIH), and ectopic ACTH secretion (EAS). In contrast, in non-pregnant populations, Cushing's disease is the leading cause, responsible for 58-70% of cases, while adrenal adenomas account for only about 15%. The reason for this difference remains unclear, but one hypothesis is that pituitary adenomas may secrete excessive levels of both cortisol and androgens, whereas adrenal adenomas primarily secrete cortisol. This difference could make it more difficult for patients with Cushing's disease to conceive, resulting in a higher prevalence of adrenal CS in pregnant individuals [2].

Twelve years after Lindsay's study, Caimari et al. [8]. Conducted a review in 2017, summarizing 214 cases of CS in pregnancy, including 46 cases diagnosed within 12 months postpartum. Their analysis indicated that adrenal adenomas remained the primary cause at 44.1%, followed by Cushing's disease at 28.2%, adrenal carcinomas at 9.4%, and pregnancy-induced CS at 13.2%. These findings are consistent with previous analyses of the etiological factors. The study also observed a significantly higher incidence of fetal loss and miscarriages in patients with pregnancy-induced CS. Possible mechanisms include abnormal expression of LH/HCG receptors in adrenal tumor tissue, increased or mutated LH receptor gene expression, and elevated HCG levels during pregnancy, leading to excessive cortisol production [21, 22]. During pregnancy, there is a general activation of the hypothalamic-pituitary-adrenal (HPA) axis, resulting in physiological hypercortisolism without specific clinical manifestations. The hepatic production of corticosteroid-binding globulin (CBG) rises 2-3 times, peaking in late pregnancy due to the effects of estrogen, which persist until delivery [23]. Additionally, the substantial increase in corticotropin-releasing hormone (CRH), mostly originating from the placenta, and ACTH secretion during pregnancy further elevates serum cortisol levels. Furthermore, the significant rise in corticotropin- releasing hormone (CRH), primarily produced by the placenta, along with increased ACTH secretion during pregnancy, further boosts serum cortisol levels [24].

4. Clinical Features and Complications of CS in Pregnancy

The typical clinical manifestations of CS during pregnancy resemble those seen in non-pregnant patients, including a Cushingoid appearance, weight gain, central obesity, and sodium retention. However, the overlap between pregnancy symptoms and those of cortisol excess such as fatigue, acne, hirsutism, weight gain, and mood disorders—can result in the clinical features being overlooked [25]. Unique clinical features of CS during pregnancy include stretch marks in areas beyond the abdomen, more pronounced striae than typical, thinning of the skin leading to increased susceptibility to abrasions, spontaneous fractures, and proximal muscle weakness [26]. Elevated cortisol levels during pregnancy in Cushing's syndrome (CS) can have severe adverse effects on both the mother and the fetus. For pregnant women, potential complications include hypertension, diabetes or glucose intolerance, preeclampsia, osteoporosis or fractures, heart failure, mental health issues, and wound infections, all of which can significantly increase the maternal mortality rate [27]. Studies indicate that patients with active Cushing's syndrome (CS) during pregnancy experience a higher incidence of certain complications compared to those with resolved CS. Specifically, active CS pa-

tients have a significantly greater incidence of gestational diabetes (36.9% vs. 2.3%), pregnancy-induced hypertension (40.5% vs. 2.3%), and preeclampsia (26.3% vs. 2.3%). This data underscores the increased risk associated with active CS during pregnancy [8]. For the fetus, although it is generally believed that 11-β hydroxysteroid dehydrogenase type 2 (11-β HSD2) in the placenta can extensively metabolize cortisol and shield the fetus from the effects of hypercortisolism, there are still potential risks [28]. A meta-analysis indicates that Cushing's syndrome (CS) patients still face a significantly increased rate of premature births and related complications. These complications include stillbirth, spontaneous abortion, intrauterine growth restriction, adrenal insufficiency in the fetus, and fetal malformations. Consequently, new borns may experience postpartum issues such as intraventricular hemorrhage, infections, and respiratory distress, which can lead to increased neonatal mortality [20, 27]. Recent studies indicate that endocrine disruptors and maternal mental health disorders may decrease the activity of 11-β HSD2 [29].

Literature indicates that pregnant women with active Cushing's syndrome (CS) experience a higher rate of premature delivery, likely due to an increased incidence of complications such as gestational diabetes, hypertension, and preeclampsia. Moreover, compared to those with resolved CS during pregnancy, active CS is associated with a higher rate of cesarean sections (51.7% vs. 21.9%) and nearly three times the miscarriage rate (24% vs. 8.5%) [8]. Moreover, pregnant patients with CS are susceptible to hypokalemia. This drop in potassium may be attributed to a deficiency in the 11-β HSD2 enzyme, which reduces the conversion of cortisol to its inactive form, 17-hydroxycortisone (cortisone). Consequently, cortisol binds more to mineralocorticoid receptors, leading to increased potassium excretion [30].CS often leads to a hypercoagulable state. Reports indicate that the risk of venous thromboembolism (VTE) in CS patients is approximately 18 times higher than in the general population [31], due to increased levels of plasma procoagulant factors and impaired fibrinolysis [32]. A recent cohort study involving 208 CS patients (89.4% with a pituitary origin) found an overall thrombosis rate of 18% [33]. %. The risk of thrombosis during pregnancy is also elevated, suggesting that pregnant women with CS may face an even higher risk. Preventive measures for thrombosis could help reduce the postoperative risk of VTE, but there is no current consensus on how to accurately identify CS patients at risk for VTE during the perioperative period or how to intervene effectively. Additionally, there is no data on the benefits and safety of thrombosis prevention for pregnant women with CS%. Moreover, CS is frequently associated with emotional and cognitive disorders that can significantly affect the patient's quality of life. These issues may persist even after biochemical remission of CS [34]. Therefore, addressing emotional concerns in pregnant women with CS is important.

5. Diagnosis of CS in Pregnancy

There are no established standards for diagnosing Cushing's syndrome (CS) during pregnancy. Typically, the diagnosis involves a combination of endocrine laboratory tests and imaging studies to confirm CS and identify the underlying causes. According to the 2008 guidelines from the International Endocrine Society, which remain in use today, initial screening should include one of the following tests: at least two 24-hour urine-free cortisol measurements, a 1 mg overnight dexamethasone suppression test, or at least two late-night salivary cortisol measurements [35]. In 2011, experts recommended using the serum cortisol diurnal rhythm test as the primary screening method for CS instead of the 1 mg overnight dexamethasone suppression test. If the initial screening yields abnormal results, a confirmatory diagnosis can be made using either the 1 mg overnight dexamethasone suppression test or a classical low-dose dexamethasone suppression test. Persistent lack of cortisol suppression would suggest the presence of CS [2]. In 2021, the International Pituitary Association advised a thorough evaluation for patients with CS, which should encompass a detailed medical history, physical examination, evaluation of clinical symptoms and signs, laboratory tests, as well as pituitary magnetic resonance imaging (MRI), and other imaging studies [36]. Plasma ACTH measurement helps distinguish between ACTH-dependent and ACTH-independent Cushing's syndrome (CS). High-dose dexamethasone suppression tests, CRH stimulation tests, and desmopressin stimulation tests are primarily used to differentiate between Cushing's disease and ectopic ACTH syndrome. Imaging studies such as pituitary MRI, adrenal CT, MRI, and color ultrasound are employed to identify tumor-like lesions in the pituitary, adrenal glands, and surrounding areas. If adrenal CS is suspected based on suppressed or low-normal ACTH levels, an adrenal ultrasound may be conducted. However, non-contrast-enhanced MRI is considered the best method for evaluating adrenal masses. Bilateral inferior petrosal sinus sampling (BIPSS) for measuring ACTH levels is regarded as the gold standard for confirming Cushing's disease. Less common imaging techniques, such as PET or PET- CT, may also be useful for detecting neuroendocrine tumors [8]. Figure 1: Demonstrates the key differences between normal Cushing's syndrome and Cushing's syndrome during pregnancy. During pregnancy, the use of laboratory tests to evaluate cortisol levels has limitations. Normal pregnancy causes elevated levels of blood cortisol, urinary free cortisol, blood ACTH, blood CRH, blood CBG, and salivary cortisol, due to the placental secretion of CRH, ACTH, and CBG. These levels reach their peak in the mid to late stages of pregnancy [22], Some reports also suggest that blood ACTH levels may be lower during pregnancy [27, 37]. Serum-free cortisol and total cortisol levels rise significantly, with plasma total cortisol increasing to 2-3 times the normal non-pregnant level, [38, 39]. while free cortisol may increase 2-4 times, and 24-hour urine cortisol can be up to 3 times the normal value in late pregnancy

[40]. Despite these increases, the diurnal rhythm of cortisol secretion remains. The effectiveness of dexamethasone in suppressing cortisol is reduced during pregnancy, which makes the 1 mg overnight dexamethasone suppression test unreliable due to the risk of false-positive results. In summary, the dexamethasone suppression test might not effectively suppress cortisol secretion, and elevated levels of 24-hour urine cortisol or salivary cortisol during normal pregnancy can easily result in false-positive results. Given that the diurnal rhythm of cortisol secretion is preserved during pregnancy, despite higher cortisol levels, measuring midnight salivary cortisol or midnight serum cortisol is recommended for diagnostic screening. The current diagnostic criteria for Cushing's syndrome (CS) during pregnancy are based on empirical evidence. The 2021 update from the International Pituitary Association's guidelines suggests that elevated urine cortisol levels more than three times the normal value and the loss of the diurnal cortisol rhythm in mid to late pregnancy may indicate CS [36]. This should be complemented by additional diagnostic imaging for confirmation. After confirming Cushing's syndrome (CS), determining the source through biochemical testing is also challenging, and limited data supports the use of high-dose dexamethasone suppression tests (HDDST) and CRH or DDAVP stimulation tests. Given the risks associated with PET and CT scans due to their radioactivity, and the potential teratogenic effects of MRI contrast agents, these methods are generally avoided during pregnancy. Therefore, renal ultrasound is preferred for screening adrenal tumors. Although the safety of plain MRI scans for the fetus has not been fully established, they should still be used when necessary to diagnose suspected pituitary tumors in pregnant [41]. Most cases reported both domestically and internationally show a significant reduction in ACTH levels in pregnant individuals with Cushing's syndrome [22, 42, 43]. However, there are a few instances where ACTH levels are markedly higher than the upper limit of the reference range (60 pg/ml, with a reference range of 5-27 pg/ml) [44]. If there's a suspicion of a pituitary origin based on high-normal to elevated ACTH levels, a pituitary MRI can be performed (without contrast, to avoid the potential effects of gadolinium contrast agents on maternal renal function or fetal development). However, many ACTH-secreting adenomas might be small and could be missed. Given the lack of substantial evidence of significant adverse effects, deciding to use contrast-enhanced MRI during pregnancy should involve a careful evaluation of the benefits versus potential risks. There are reports of patients in early pregnancy suspected of having Cushing's syndrome who were definitively diagnosed using high-resolution contrast-enhanced MRI and bilateral inferior petrosal sinus sampling (BIPSS). These patients were able to deliver successfully after surgical treatment, with normal fetal development observed at a 3-month follow-up [44]. However, due to the increased risk of radiation exposure and venous thrombosis, BIPSS is generally not recommended during pregnancy.

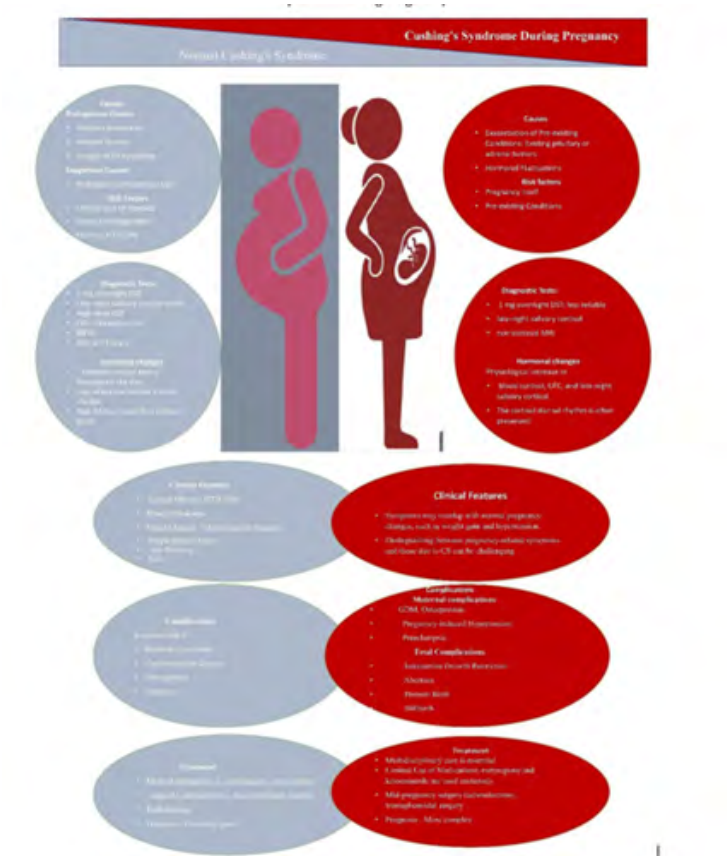

Figure 1: Highlighting the key Difference Between Normal Cushing' s Syndrome and Cushing's Syndrome During Pregnancy.

Table 1: Challenges and Advances in the Diagnosis and Treatment of Cushing's Syndrome in the First Trimester.

Challenges	Advances	Complications
Physiological Changes: Increased cortisol production in normal pregnancy Limited Diagnostic Tools: Standard tests like 24-hour UFC and late-night salivary cortisol have altered reference ranges. Risk of Teratogenicity: Most medications pose risks to the fetus. Avoidance of Surgery: High risk of miscarriage and congenital malformations	Improved Diagnostic Criteria: Pregnancy-specific cortisol reference ranges Safer Medical Therapies: Use of metyrapone with lower fetal risk. Non-Invasive Imaging: MRI for better tumor visualization without radiation.	Maternal Complications: □ Miscarriage □ Severe Hypertension □ Infections □ Fetal Complications: □ Congenital Malformations □ Fetal Growth Retardation

Note: UFC, Urinary Free Cortisol; MRI, Magnetic Resonance Imaging.

Table 2: Challenges and Advances in the Diagnosis and Treatment of Cushing's Syndrome in 2nd Trimester.

Challenges	Advances	Complications
Ongoing Hormonal Shifts: Continued interference with diagnostic accuracy. Fetal Monitoring: Need for continuous assessment of fetal development. Balancing Risks: Deciding between conservative management and aggressive treatments. Surgical Timing: Balancing surgery timing to minimize risks.	Enhanced Imaging: High- resolution MRI for better tumor detection. Optimized Surgery: Improved techniques and minimally invasive procedures. Safer Surgical Interventions: Lower risk of complications.	Maternal Complications: □ Gestational Diabetes □ Pre-eclampsia □ Osteoporosis Fetal Complications: □ Preterm Labor □ Fetal Growth Restriction

Table 3: Challenges and Advances in the Diagnosis and Treatment of Cushing's Syndrome in 3rd Trimester.

Challenges	Advances	Complications
Late Gestation Changes: Difficulty distinguishing between normal pregnancy symptoms and Cushing's exacerbations. Delivery Planning: Coordinating timing and method for optimal outcomes. Postpartum Complications: Managing potential adrenal insufficiency in the newborn.	Research and Education: Increased understanding and better management guidelines. Patient Support: Improved education and support systems for pregnant women.	Maternal Complications: □ Worsening Hypertension □ Diabetes Complications □ Cardiovascular Issues Fetal Complications: □ Preterm Birth □ Adrenal Insufficiency

Table 4: Challenges and Advances in the Diagnosis and Treatment of Cushing's Syndrome in Postpartum.

Challenges	Advances	Complications
Hormonal Fluctuations: Overlapping symptoms with normal postpartum recovery and breastfeeding impact cortisol levels. Diagnostic Difficulties: Symptoms overlap with postpartum conditions and persistent elevated cortisol levels from pregnancy. Treatment Complications: Medication risks for breastfeeding infants and surgical risks during postpartum recovery. Patient Compliance: Demands of newborn care and mental health issues.	Improved Diagnostic Criteria: Postpartum-specific cortisol reference ranges. Advanced, non-invasive imaging techniques (MRI): Safe Medical Therapies: Enhanced Surgical Techniques: Minimally invasive procedures and optimized timing for surgical interventions. Multidisciplinary Care: Integrated care teams with endocrinologists, obstetricians, and pediatricians. Increased postpartum support services. Patient Education and Support:	Maternal Complications: □ Persistent Hypertension □ Diabetes Mellitus: □ Infections □ Osteoporosis □ Psychological Effects □ Delayed Recovery Fetal/Neonatal Complications: □ Adrenal Insufficiency □ Growth and Development Issues □ Preterm Birth □ Neonatal Intensive Care □ Breastfeeding Challenges □ Long-term Health Monitoring

6. Advances in the Treatment of CS in Pregnancy

Treatment for Cushing's syndrome (CS) during pregnancy involves both medical and surgical options. Surgery is usually best performed during mid-pregnancy, as early surgery poses a higher risk of miscarriage, and the fetus may be affected by various medications. According to a 2011 expert consensus, surgical intervention, including the removal of pituitary and adrenal tumors, is recommended before the last trimester. There is a reported case of unilateral adrenal cortex tumor resection at 25 weeks of gestation, with a favorable outcome for both the mother and baby after 10 years of follow-up [45]. Recently, we published a report on Cushing's syndrome during pregnancy, highlighting two cases [46]. In the first case, a female patient underwent a successful unilateral laparoscopic adrenalectomy at 32 weeks of gestation, with no surgical complications. She subsequently delivered a healthy baby at 39 weeks via normal delivery. Nine months after delivery, the patient remains in continuous remission. In the second case, the patient delivered twin boys via cesarean section at 33 weeks gestation. The infants required 10 days of intensive care and home feeding for one month. During a follow-up visit, the patient underwent a successful laparoscopic adrenalectomy. Two months post-surgery, both the mother and her twin sons are thriving and well-developed. Fewer than 100 cases of endogenous Cushing's syndrome (CS) treated during pregnancy have been reported, with treatments including surgery (24%), medical therapy (11%), or a combination of both (4.7%)(47). Medical treatments for CS involve steroid synthesis inhibitors such as metyrapone and ketoconazole, as well as the glucocorticoid receptor antagonist mitotane. Since these medications can cross the placental barrier and potentially harm the fetus, they are rarely used during pregnancy. At present, no medications are approved for use during pregnancy. In a systematic review of women diagnosed with CS during pregnancy, 61 patients underwent surgery at a median gestational age of 21 weeks [range: 17-26 weeks]. Among these, 11 had transsphenoidal surgery (TSS), 44 had adrenalectomy, and 6 had bilateral adrenalectomy. Remission was achieved in 77% of the cases, 12% remained active, and 10% had no available data. For those who achieved remission post- surgery, the rates of fetal loss (6.7% vs. 28.6%), preterm birth (56.1% vs. 80%), and low birth weight (70.6% vs. 100%) were lower compared to those who did not achieve remission [8]. According to Francisca's summary, of the patients with CS treated during pregnancy, 24 received medical treatment, and 49 underwent surgery. The overall fetal loss rates were 20.8% for those receiving medical treatment and 12.5% for those undergoing surgery, both significantly lower than the 30.6% rate observed in 128 untreated patients ($p=0.021$). However, neither treatment method had a significant impact on the rates of preterm birth and low birth weight ($p>0.1$), and no medication-related adverse events were reported [8]. So far, only 11 cases of medical treatment for CS during pregnancy have been reported. The most frequently used medications in these cases are cabergoline, ketoconazole, and metyrapone [13]. Metyrapone lowers cortisol production by inhibiting 11-β hydroxylase in the cortisol synthesis pathway. It may exacerbate hypertension and/or lower potassium levels, so regular monitoring of blood pressure and potassium is necessary. A recent case involved a pregnant patient with CS due to an adrenal cortex tumor who was treated with a combination of metyrapone (0.5g three times daily) and ketoconazole (0.4g twice daily). The patient declined surgery and continued the medication throughout the pregnancy without complications. She delivered a

healthy baby via cesarean section and had the tumor resected postpartum, with a positive outcome observed at a 5-year follow-up [48]. There are reports of cabergoline being used in Cushing's syndrome cases with positive outcomes for both mother and fetus. However, it may result in difficulties with breastfeeding after delivery (49, 50). Ketoconazole is another treatment option, but there is limited information about its safety and efficacy during pregnancy [6]. Likewise, data on the use of pasireotide and osilodrostat during pregnancy are also inadequate [13].

In conclusion, while medical treatment for CS during pregnancy is not an absolute contraindication, it may be considered when surgery is not feasible or for managing symptoms around the time of surgery. Such treatments can potentially lower the risk of fetal death but do not address preterm birth or intrauterine growth restriction. The impact of treatment on overall maternal mortality remains uncertain due to surgical risks, and with the limited number of cases, there is no definitive approach for managing pregnancy-induced CS.

7. Follow-up and Monitoring of CS in Pregnancy

Follow-up for pregnant women with CS is essential. Cortisol excess should be re-evaluated after delivery. While the HPA axis activation due to pregnancy typically resolves within days to weeks postpartum, full normalization of dexamethasone's effect on cortisol may take 4-6 weeks, with CBG levels rising within three months. Women with Cushing's Disease should generally have their postpartum condition reassessed 2-3 months after delivery if they have not used steroid synthesis inhibitors, pasireotide, or cabergoline. Those not on these medications are usually allowed to breastfeed. The International Pituitary Association's 2021 guidelines recommend lifelong monitoring for Cushing's Disease recurrence. Regular annual assessments of HPA function, using tests such as late-night salivary cortisol, dexamethasone suppression test, urinary-free cortisol, and DDAVP tests, are advised for detecting recurrences. In China, DST may be preferred for monitoring HPA axis function.

8. Conclusion

In summary, diagnosing and treating Cushing's syndrome during pregnancy presents considerable challenges due to physiological changes and potential risks to the fetus. Nevertheless, advances in diagnostic techniques, safer medical therapies, and surgical approaches, along with a multidisciplinary strategy, have significantly improved outcomes for both mothers and their babies. The complications associated with Cushing's syndrome can vary by trimester and have a major impact on maternal and fetal health, underscoring the importance of vigilant monitoring and management throughout pregnancy. For screening pregnancy-induced Cushing's syndrome, initial tests should include measurements of urinary free cortisol, late-night salivary cortisol, and the 1 mg overnight dexamethasone suppression test, with attention to potential false negatives. It is crucial to identify and manage complications and comorbidities to ensure the safety of both mother and fetus. Mid-pregnancy surgery is typically recommended as the primary treatment, though supporting evidence is limited. Pregnant women with active Cushing's disease or those undergoing medical treatment should be managed by a multidisciplinary team, including obstetricians, pituitary specialists, neonatologists, and experts in endocrine metabolism, neurosurgery, and urology. West China Hospital of Sichuan University is implementing a multidisciplinary team (MDT) approach to improve the diagnosis, treatment, and follow-up of Cushing's syndrome, including cases related to pregnancy.

9. Funding

This study was supported by a clinical research incubation project of the 1-3-5 plan for discipline excellence development at West China Hospital, Sichuan University (Grant number). (No.2020HX-FH034).

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