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Mini-Review

Hyperparathyroidism during pregnancy, a mini review to complications and treatments

Fateme Sharafeddin, Golnaz Goudarzi*

Abstract

Hyperparathyroidism (HPT) is one of the most common endocrine disorders, however it is a rare disease during pregnancy with notable maternal and fetal morbidity and mortality. We investigated 46 articles in PubMed database that seven articles focused on this topic. This review will examine the maternal and neonatal complications and the options for managing and treating this disease during pregnancy.

Keywords: Hyperparathyroidism, Pregnancy, Treatment, Complications, Surgery, Parathyroidectomy, Conservative, Hypercalcemia, Calcium, Neonate

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Introduction

Hyperparathyroidism (HPT) is a common endocrine disorder; however it is rare during pregnancy, affecting only 0.05% of reproductive-age women. Diagnosing the condition can be difficult due to low awareness, non-specific symptoms, and similar symptoms to those of a normal pregnancy such as nausea, vomiting, and fatigue. If left untreated, HPT during pregnancy can lead to increased health risks for both the mother and fetus. Deciding on the appropriate treatment is therefore crucial. We investigated 46 articles published in PubMed database with the keywords of Hyperparathyroidism, Pregnancy, and Treatment since 2020. Seven articles focused on our topic, and we reviewed them. All seven articles were case report studies.

Cases and their information

In 2020, Davis and colleagues reported a case of a 35-year-old woman from Bangladesh who had high levels of serum-corrected calcium (3.6 mmol/L, with a normal range of 2.15-2.55 mmol/L), parathyroid hormone (20.8 p mol/L, with a normal range of 1.0-7.0 pmol/L), and 24-hour urine calcium (8.24 mmol/L). She underwent surgery to remove her left inferior parathyroid gland, which normalized her serum calcium levels. However, she developed pre-eclampsia in her 30th week of pregnancy. The neonate had normal calcium levels at birth, but was admitted to the neonatal intensive care unit (ICU) for nine weeks due to low birth weight, jaundice, hypoglycemia, and retinopathy of prematurity. On the 19th day of life, the neonate developed hypercalcemia (1).

In 2020, Sharma and colleagues conducted a study on a 31-year-old woman who was pregnant for the first time (G1P0) in Louisiana State. She presented with symptoms of nausea, vomiting, polyuria, constipation, and weakness at six weeks of gestation and had a high level of parathyroid hormone (PTH) at 850.5 pg/mL (normal range: 18.5-88 pg/mL). The patient was initially treated with calcitonin and aggressive intravenous fluid therapy, although she developed a tolerance to calcitonin. Her corrected calcium levels were also high, ranging from 11.1 to 13.3 mg/dL. Bisphosphonate and cinacalcet were not prescribed due to concerns about possible fetal complications. At the 8th week of gestation, the patient underwent surgery to remove her right inferior parathyroid gland, which normalized her calcium levels and ensured normal fetal development and growth. However, at the gestational age of 26w6d, the patient developed pre-eclampsia and had to deliver her baby boy by C-section. Fortunately, the newborn's calcium, phosphorus, and alkaline phosphatase levels were all within the normal range, and he had an uneventful stay in the neonatal ICU. He was discharged with normal calcium levels at two months of age (2).

In 2021 Latif et al studied two pregnant women that were diagnosed with primary hyperparathyroidism (PHPT). The first patient experienced epigastric pain, nausea, and vomiting at 30 weeks of pregnancy, and testing revealed high levels of serum PTH, urinary calcium excretion, and

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Clinical Research Development Center, Najafabad Branch, Islamic Azad University, Najafabad, Iran.
***Corresponding author:** Golnaz Goudarzi, Email: Golnazgoudarzi80@gmail.com

Implication for health policy/practice/research/ medical education

Hyperparathyroidism is a rare disease during pregnancy with notable maternal and fetal morbidity and mortality. Complications of this disease and treatment options are controversial.

hypercalcemia, which led to a diagnosis of PHPT. Despite initial treatment with intravenous hydration, calcitonin, and cinacalcet, her calcium levels remained elevated, and she underwent a right inferior parathyroidectomy. After the surgery, her calcium levels normalized, and she gave birth to a healthy baby girl via spontaneous vaginal delivery six weeks later. The second patient presented to the emergency department with concerns about decreased fetal movements and non-reassuring fetal heart tones at 30 weeks of gestation and required an emergency cesarean section. After delivery, she developed polyuria and tremors and was diagnosed with PHPT. She received aggressive intravenous fluid resuscitation, calcitonin, and cinacalcet, which normalized her calcium levels after five days. She then underwent a left inferior parathyroidectomy on the 7th day of hospitalization and was discharged on the 10th day with normal serum calcium levels. The newborn required a short stay in the neonatal intensive care unit due to hypoglycemia but was reported to be doing well (3).

In 2021, Tsai and colleagues conducted a study on a 31-year-old woman who experienced severe pain in her upper abdomen at 15 weeks into her pregnancy. She had nausea, vomiting, increased urination, and felt generally unwell. The woman was treated with fasting, intravenous fluids, electrolyte replacement, painkillers, and anti-nausea medication, which helped to relieve her abdominal pain and restore her potassium levels to normal. However, her serum calcium level remained high at over 12 mg/dL. Further tests showed that her PTH level was elevated, while her 25-hydroxyvitamin D level was low. A team of specialists decided to proceed with surgery, and seven days after being admitted to the hospital, the woman underwent an operation to remove an enlarged left inferior adenomatous parathyroid tumor that was adhered to her thyroid gland. The surgery was successful, and her calcium and PTH levels rapidly returned to normal. However, the next day her calcium level dropped to 8.4 mg/dL, indicating a condition called "hungry bone syndrome". She was discharged from the hospital on the fifth day after the surgery, with her serum calcium and PTH levels under control. She went on to have an uneventful pregnancy and delivered a healthy baby with no signs of low blood calcium levels (4).

In 2021, Xu et al reported a case study of a 31-year-old woman in China who had a history of hypercalcemia for three years and nephrolithiasis for over two years. The patient did not have a family history of hypercalcemia or endocrine tumors. Upon physical examination, a round mass measuring 20mm x 30mm was found in the patient's left lower leg, which was deep-seated, immobile, and painless. Laboratory tests revealed that the patient had high serum calcium levels (3.84 mmol/L) and PTH levels (1393 pg/mL), which were above the normal reference range (2.20-2.65 mmol/L and 15-65pg/mL, respectively). An ultrasound scan showed a single solid nodule measuring 22.4 mm × 7.8 mm in the left lower lobe of the thyroid gland, indicating the presence of parathyroid adenoma. The adenoma was successfully removed without any complications for both the mother and fetus. At 38 weeks of pregnancy, the patient delivered a healthy female infant weighing 2700 g, and both mother and infant had normal calcium levels in the postpartum period. The patient was discharged three days after delivery in a stable and satisfactory condition (5).

In 2022, Chung et al studied a 31-year-old nulliparous woman in South Korea. Her blood test at the 11th week of gestation results showed that the serum calcium level was elevated to 12.9 mg/dL (reference range: 8.8-10.6), and the PTH level was raised to 157 pg/mL (reference range: 15.0-65.0). There were no changes in the serum calcium levels after several weeks of conservative treatment. Thus, the multidisciplinary team planned the surgery at 11 weeks of gestational age (the first trimester). She was released from the hospital on postoperative day 2. A follow-up examination on postoperative day 8 showed the calcium level became normal. A healthy male neonate of 2910 g was delivered vaginally at 38 weeks gestation, and his postpartum period was uneventful (6).

Pliakos et al conducted a study in Japan in 2022 on a 34-year-old woman who was in her 25th week of pregnancy. The woman experienced severe vomiting during her second trimester and was found to have high levels of ionized serum calcium (1.47 mmol/L) and PTH (75.8 pg/mL), which were higher than the normal range (1.15-1.33 mmol/L and 15-65 pg/mL, respectively). The woman underwent a surgery called parathyroidectomy to remove an enlarged right superior parathyroid gland. The levels of thyroid hormone before and after the surgery were 176.9 and 30.29 pg/dL, respectively. The woman and her baby had a smooth recovery after the surgery. Her postoperative laboratory results showed that her serum calcium level was 9.4 mg/dL, PTH level was 5.59 pg/dL, and phosphorus level was 3.3 mg/dL after 8 hours. She was given intravenous calcium supplementation and oral calcium and vitamin D3 supplements. The woman had a normal vaginal delivery and both she and her baby had normal levels of calcium during their follow-up period (7).

Discussion

From the study of the relevant cases and the authors' research, we found that neonatal complications include

hypocalcemia due to parathyroid suppression (2,8,9), low birth weight (8), high risk of prematurity(8,10), tetany (8,9), intrauterine growth restriction and a three to five times increased risk of miscarriage (10). On the other hand, HPT during pregnancy causes some maternal complications. Some studies demonstrated that this disorder causes hypercalcemic crisis (10,11). It is shown that hypercalcemic crisis is associated with nausea, vomiting, mental status changes, dehydration, uremia and coma (12-14). Furthermore, it is reported that altered mental status or seizure may develop in extreme cases of hypercalcemic crisis (9). Nephrolithiasis (10), pre-eclampsia (8,10), increase the risk of perinatal morbidity and mortality (15) and hyperemesis gravidarum (10) are also among other maternal complications of this disorder. Pancreatitis is rare and virtually not seen in patients with mild hypercalcemia (16).

There are different treatment options available for HPT during pregnancy, including medical and surgical approaches. Conservative treatment options include bisphosphonates, calcitonin, denosumab, cinacalcet, fluid resuscitation, low calcium intake, and vitamin D supplementation. However, bisphosphonates and denosumab are contraindicated in pregnancy due to potential risks to the fetus (17), while calcitonin has short-lived benefits and may lead to tachyphylaxis (12). Parathyroidectomy is considered the treatment of choice for women with HPT during pregnancy, especially when serum calcium levels exceed 11.4 to 12 mg/dL (3). Surgery is generally recommended during the second trimester of pregnancy (18), and there are reports of successful outcomes in both the mother and the fetus. Conservative treatment can be used for mild cases, nonetheless parathyroidectomy may be necessary for cases that do not respond to medical treatment. The decision to perform surgery and the timing of surgery should be based on the individual patient's case and serum calcium levels.

Conclusion

We concluded that HPT in pregnancy, which is a rare disease, leads to maternal, fetal and neonatal complications if not controlled and treated. In mild cases, conservative treatment is the answer, however surgery is the best treatment when conservative treatment failed, although it should be noted that serum calcium level and the time of surgery are important.

Authors' contribution

Conceptualization: GG.
Methodology: FS.
Validation: FS, GG.
Formal analysis: FS, GG.
Investigation: FS, GG.
Resources: FS.
Data curation: FS.
Writing–original draft preparation: FS.
Writing–review and editing: FS, GG.
Visualization: GG.
Supervision: FS.
Project Administration: FS.
Funding Acquisition: GG.

Conflicts of interest

The authors declare that they have no competing interests.

Ethical issues

Ethical issues (including plagiarism, data fabrication, double publication) have been completely observed by the authors.

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