Royal Hospital for Women (RHW)
BUSINESS RULE
COVER SHEET

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SUMMARY	To guide the clinicians on the management of neonates born to women with hyperparathyroidism

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Maternal hyperparathyroidism – Neonatal care RHW CLIN026

1. BACKGROUND

Maternal hyperparathyroidism, if untreated or undiagnosed, can lead to maternal hypercalcemia. High influx of calcium to fetus through placenta can suppress fetal parathyroid activity. This may result in severe hypocalcaemia leading to seizures in neonate. This CBR aims at identifying and screening infants who are at risk for hypocalcemia secondary to maternal primary hyperparathyroidism (PHP).

2. RESPONSIBILITIES

Medical and Nursing/ Midwifery Staff

3. PROCEDURE

3.1 Equipment

3.2 Clinical Practice

1. Obtain detailed maternal history including:
    a. Duration and severity of hypercalcemia, defined as serum calcium >0.25 mmol/L above the upper limit of normal.(1)
    b. Any known aetiology for maternal hypercalcemia/maternal hyperparathyroidism, e.g. parathyroid adenoma, parathyroid hyperplasia, parathyroid carcinoma, multiple endocrine neoplasia syndrome
    c. Any treatment being given to control hypercalcemia/hyperparathyroidism
    d. Latest ionised and total serum calcium prior to delivery
2. Measure serum ionised and total calcium, phosphorus, magnesium, alkaline phosphatase and parathyroid hormone (PTH) at 24 hours of life. If normal, measure **either** of the following at 72 hours of age: (1) ionised Ca on capillary gas **or** (2) serum ionised, total and corrected calcium.
3. If 24 and 72 hour serum calcium measurements are normal – no further follow up is required.
4. If serum calcium is low at 24 hour or 72 hour samples -
    a. Take a history and examine for any clinical symptoms/signs of hypocalcemia (e.g. seizures, jerky movements, jitteriness, irritability (2)
    b. Discuss with neonatologist/paediatric endocrinologist on further monitoring and management, including Calcium supplementation
    c. Advise parents of symptoms to watch for.
    d. Ongoing monitoring to be advised by neonatologist/paediatric endocrinologist.

4. ABORIGINAL HEALTH IMPACT STATEMENT DOCUMENTATION

Considerations for culturally safe and appropriate care provision have been made in the development of this Business Rule and will be accounted for in its implementation.

5. EDUCATIONAL NOTES

- Hypercalcemia in pregnancy is rare and in >90% of cases primary hyperparathyroidism (PHPT) is the cause of it. The prevalence of PHPT in general population is estimated to be ~0.5%, but the incidence in pregnancy is unknown and uncommon. The diagnosis is based on persistent hypercalcemia in the presence of increased parathyroid hormone (PTH) or a PTH level inappropriate for the level of serum calcium.(1) However, it is difficult to make an early diagnosis during pregnancy as the symptoms are usually subtle and are easily confused with other minor complications of pregnancy. The majority of patients with primary hyperparathyroidism have mild hypercalcemia, while about 5% of them are normocalcemic.(1-4)
- The most common causes of primary hyperparathyroidism in pregnancy are single parathyroid adenoma (80%), parathyroid gland hyperplasia (15%), multiple adenomas (3%) and parathyroid carcinomas (1%).(1, 5)
- The diagnosis of primary hyperparathyroidism may be easily missed during pregnancy, owing to its non-specific presentation. A high index of suspicion and measurement of ionized calcium levels is encouraged, especially for patients with excessive nausea and vomiting, nephrolithiasis, atypical presentations of hypertensive disorders, or isolated polyhydramnios.(5)
- Fetal complications: Early literarure suggests, in mothers with primary hyperparathyroidism who were not treated and probably with severe maternal hypercalcemia, the incidence of a fetal complication can be as high as 80%. Even in conservatively managed patients, the incidence of a neonatal complication has been reported to be as high as 53%, of which 27% to 31% is neonatal death. Other complications include intrauterine growth restriction, low birth weight, preterm delivery, and intrauterine fetal demise.(6) More recent literature suggests lower complication rates and good treatment outcomes, when the maternal hypercalcemia is only mild to moderate.(5-7)
- **Pathogenesis of neonatal hypocalcemia:** Neonatal hypocalcemia is the most common complication in neonate. Elevated maternal serum calcium leads to hypercalcemia in the fetus, which causes fetal parathyroid gland suppression. After delivery, these glands are still suppressed causing hypocalcemia, which is usually transient (lasting up to 3–5 months after birth).(4) Neonatal hypocalcemia is related to levels of maternal hypercalcemia.(1)
- The timing of hypocalcaemia in relation to birth is unclear, as whilst case reports suggest hypocalcemia can be late onset (after 72 hours of life), (2, 7, 8) these case reports may reflect the timing of biochemical testing rather than actual abnormalities. The incidence of hypocalcemia was suggested as high as 50% in infants born to untreated mothers.(7)
- Symptoms of hypocalcemia include neuromuscular irritability, myoclonic jerks, jitteriness, seizures, and cardiac involvement such as tachycardia, heart failure, prolonged QT interval, decreased contractibility.(2) These neonates do well if calcium supplementation is started promptly. Hypocalcemia can persist for several months and in most bot not all cases resolves.(5-7)
- RHW-SCH endocrine consensus: Published literature, mostly case reports, suggest neonatal hypocalcemia associated with maternal hyperparathyroidism may have a delayed presentation. However in these case reports, serum calcium was not measured

prior to clinical presentation and the 'late presentations (i.e. with seizures)', were likely because of undetected/asymptomatic earlier hypocalcemia.

6. ABBREVIATIONS

PHPT	Primary hyperparathyroidism		
PTH	Parathyroid hormone		

7. REFERENCES

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8. REVISION AND APPROVAL HISTORY

Date	Revision No.	Author and Approval
21.2.24	1	Endorsed RHW SQC