

CASE REPORT

# Case Report: Hypercalcaemia due to Primary Hyperparathyroidism in Pregnancy

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## Abstract

A 34-year-old pregnant patient presented at 6 weeks gestation for routine biochemistry tests with elevated serum calcium levels (measured Ca 2.78 mmol/L and calculated Ca 2.64 mmol/L; RI 2.10 to 2.60 mmol/L) with normal serum albumin (47 g/L; RI 37 – 48 g/L). Subsequent presentations showed persisting high Ca and ionised Ca, with normal serum parathyroid hormone (PTH) (2.7 pmol/L; RI 1.5 – 7.5 pmol/L), serum PO<sub>4</sub>, vitamin D and normal renal markers. Urine Ca excretion was within reference limits. Following an early miscarriage serum Ca levels normalised while PTH progressively increased. (5.6 at 9 weeks gestation and 7.7 at 13 weeks gestation (1.5 – 75 pmol/L)). A parathyroid adenoma was diagnosed on imaging and a left superior parathyroidectomy was performed. Post-operative blood results suggested resolution of hyperparathyroidism. Her second pregnancy too, spontaneously aborted after 6 weeks of gestation despite Ca remaining within normal limits. Thyroid function remained normal, and there was no clinical suspicion of MEN. All other major causes of early pregnancy loss were screened for and excluded. The patient presented again in early pregnancy with no known complication and normal serum PTH (2.1 pmol/L; RI 1.5 – 7.5 pmol/L) and progressed to full term. (Figure 1) shows the measured and calculated serum Ca and PTH levels during the period of testing.

**Keywords:** hypercalcaemia, pregnancy, primary hyperparathyroidism, parathyroidectomy

## Introduction

Hypercalcaemia in pregnancy while uncommon, can cause significant maternal and foetal morbidity/mortality [1]. While Primary hyperparathyroidism (PHPT) diagnosed during pregnancy is rare, it is a leading cause of hypercalcaemia in pregnancy [2]. The most common cause of PHPT in pregnancy is reported to be a single adenoma [3]. PHPT is often underdiagnosed because PTH is not a common diagnostic test requested during pregnancy. Coupled with the lack of follow-up of hypercalcaemia in pregnant patients, may explain the low frequency of diagnosis of HPT. The following study was performed to determine the prevalence of hypercalcaemia in pregnancy and the prevalence of PHPT first presenting in pregnancy.

## Method

Community data collected within our laboratory during a 3 months period were collated to identify pregnant females who had serum biochemistry tests. Measured and calculated serum Ca results were assessed against the adult reference interval for serum Ca (2.10 – 2.60 mmol/L). Mean, median and ranges of serum measured and ionised Ca for each trimester were calculated. A student-t test was used to compare Ca values between trimesters.

## Results

A total of 1370 pregnant women were tested for routine serum biochemistry during the selected period of time. The mean age was 31.7 (SD 5.1) years with a range of 16 to 47.7 years. Serum Ca and albumin for all pregnant women are shown in (table 1). Demographic data and the biochemical data for each trimester are given in (tables 2 and 3) respectively.

A student-t test demonstrated no significant difference between patient age, serum Ca and albumin values between trimesters.

Within this cohort of women (n = 1370) only 1 patient was hypercalcaemic. She was a 32 year old woman who presented at 3 weeks of gestation with a serum measured Ca level of 2.67 mmol/L (2.10 – 2.60) and an albumin level of 47 g/L (37 – 48). Her serum 25OHD level was 46 nmol/L (50 – 160). Her history indicated hypercalcaemia during previous pregnancies. Persisting hypercalcaemia during the first 2 pregnancies were noted. Clinical notes for the second pregnancy (2.5 years following the first pregnancy) indicated pregnancy loss at 7 weeks of gestation. The

**Table 1:** Serum albumin and Ca values for all pregnant women (n=1370)

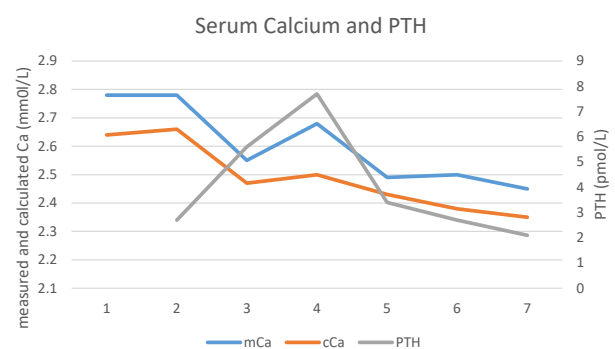
	Mean (SD)	Median	Range	Reference interval
Age (y)	32 (5)	32	16 - 48	
Serum albumin (g/L)	41 (5)	42	26 - 57	37 - 48
Measured Ca (mmol/L)	2.29 (0.09)	2.3	2.04 – 2.67	2.10 – 2.60
Calculated Ca (mmol/L)	2.27 (0.09)	2.27	2.05 – 2.6	2.10 – 2.60

**Table 2:** Demographic data for each trimester

Trimester	N	% of total pregnancies	Age (mean, SD)
1	916	67	32, 0.2
2	134	10	32, 0.4
3	320	23	32, 0.28

**Table 3:** Mean and range of serum albumin and Ca for each trimester

Trimester	Measured Ca (2.10 – 2.60 mmol/L)	Calculated Ca (2.10 – 2.60 mmol/L)	Serum albumin (37 – 48 g/L)
1	2.32 (2.09 – 2.67)	2.24 (2.05 – 2.53)	32.31
2	2.25 (2.08 – 2.46)	2.29 (2.12 – 2.50)	32.07
3	2.24 (2.04 – 2.49)	2.35 (2.13 – 2.60)	32.31



**Figure 1:** Serum measured and ionised Ca and PTH level in the patient over time. Time points 1, 2 and 3 are gestation weeks 6, 7 and 8. Time point 4 follows pregnancy loss, time point 5 was following parathyroidectomy and time point 7 is early pregnancy.

only serum PTH level was measured 7 years after the first miscarriage with hypercalcaemia, however this was within normal limits. It is unknown if the patient had surgical or medical therapy in the interim.

## Discussion

Hypercalcaemia may occur due to a variety of pathological causes. The commonest cause of hypercalcaemia during pregnancy, primary hyperparathyroidism has been reported to be a significant cause of early pregnancy loss [2]. Less common are hyperparathyroidism due to diffusely spread hyperparathyroid nodules, parathyromatosis, in the context of malignancy, MEN syndrome or chronic renal disease [4].

Hypercalcaemic pregnant women should be screened with serum PTH, and followed up appropriately. Hypercalcaemia during pregnancy has occasionally been attributed to placental PTH related protein (PTHrP) [3]. This patient may be in the category of normocalcaemic hyperparathyroidism, with rising Ca during pregnancy possibly due to other factors. Previous case series of HPT in pregnancy report 48% pregnancy loss in the first and second trimesters [2]. Early diagnosis of HPT and intervention can greatly increase the viability of pregnancy. While invasive investigations is a challenge during pregnancy, surgical and medical therapies (calcimimetic agents, bisphosphonates) are effective in reducing maternal and foetal complications [1]. Further investigations, definitive diagnosis and treatment will be missed if the patient is lost to follow up. Furthermore

it may be prudent to lower the critical Ca limit for pregnant patients, enabling immediate notification of hypercalcaemia to the requesting doctor. Perinatology Society suggests a lower reference interval for Ca in the 2<sup>nd</sup> and 3<sup>rd</sup> Trimesters while a higher ULN is suggested for the 1<sup>st</sup> trimester [5]. Our date is consistent with this suggestion, with lower median Ca noted in the second and third trimesters compared to the first, however these differences were not significant.

Biochemical results may be the only means of diagnosis of hypercalcaemia because many patients may be asymptomatic or may show symptoms consistent with hyperemesis gravidarum. Therefore the laboratory plays a pivotal role in early diagnosis of hypercalcaemia in pregnancy, and trimester specific or pregnancy serum Ca reference intervals and critical limits will be valuable in alerting clinicians enabling early intervention.

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