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Kidney stones during pregnancy: an investigation into stone composition

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Abstract Kidney stones can be a source of considerable morbidity for pregnant women. Although there is a body of literature confirming that different stone compositions predominate for different age and sex cohorts, there have been no similar reports characterizing the nature of stone disease during pregnancy. We performed a multi-institutional study to define the composition of renal calculi diagnosed during pregnancy. We retrospectively reviewed the records from two stone referral centers of all patients diagnosed with a de novo kidney stone during pregnancy who underwent a procedure for the purpose of stone removal from June 2001 through September 2007. A total of 27 patients were identified, with a mean age of 26.8 years (range, 21–34). Twenty patients (74%) had no history of prior stone formation. Seven patients (26%) had previously formed stones, although none of these patients had a known kidney stone at the time they became pregnant. Stones were removed in the first, second, third trimester and immediately post-partum in 4, 52, 22, and 22% respectively. Stone removal was performed without complication in all cases. Analysis found that in 74% of all cases (20 patients) stones were composed predominantly of calcium phosphate (hydroxyapatite). In 26% of cases, (7 patients) the stones were composed predominantly of calcium oxalate. Of the seven patients with prior stone history, three patients had previously formed calcium phosphate stones and four patients had previously formed calcium oxalate stones. Calcium oxalate calculi are the most common stone in non-pregnant women of a comparable age as our subjects. However, our present data suggest that stones detected during pregnancy are most commonly composed of calcium phosphate (hydroxyapatite). Indeed, it is the minority of stones that are composed of calcium oxalate. Although the reason for this unusual preponderance of calcium phosphate calculi is unclear, physiologic alterations that occur during pregnancy may be influential.

Keywords Kidney · Calculus · Pregnancy

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Introduction

Although urolithiasis may be an infrequent complication of pregnancy, it has been reported that approximately one in 1,500 pregnancies will be affected by this malady [1]. The morbidity associated with renal colic can be significant, and pain from this condition remains the most common non-obstetric cause for hospitalization during pregnancy [2]. Beyond the pain to the mother caused by the offending stone, though, the occurrence of such an event may adversely affect the fetus, as renal colic during pregnancy is associated with an increased risk of pre-term delivery [3].

The incidence of symptomatic urolithiasis is similar between pregnant and non-pregnant women, but the pathophysiology of stone formation in these two cohorts may differ [1]. Pregnancy induces a number of physiologic effects, including an increase in renal plasma flow, as well as an increased filtered load of sodium, calcium, and uric acid, lithogenic changes that may be offset by increased excretion of urinary inhibitors [4]. As these physiologic

changes of pregnancy are not typically encountered in the non-pregnant stone former, it is conceivable that the mechanism of stone formation, and therefore the composition of formed stones, may be different among these groups. Therefore, we performed a study to characterize the composition of kidney stones diagnosed during pregnancy and subsequently removed.

Material and methods

We undertook a retrospective analysis of all pregnant patients presenting to two stone referral centers between January 2001 and December 2007. Women who began their pregnancy with a known renal calculus were excluded from the analysis. A cohort of pregnant women with a symptomatic renal calculus who underwent a stone removal procedure was selected for further evaluation. In all cases, the stone material removed was subjected to compositional analysis. All patients underwent an extensive diagnostic evaluation, including serum creatinine assay, urinalysis and urine culture, renal and bladder ultrasound imaging, and, when, indicated, additional imaging studies including plain film X-ray or limited intravenous pyelography. Indications for surgical intervention included pain uncontrolled by analgesia, or signs of persistent obstruction or infection. All patients were treated primarily with ureteroscopy, and perioperative fetal monitoring was performed by the patient's obstetric team in all cases. In most cases, both rigid (6.9 French) and flexible (7.5 French) ureteroscopes were utilized. Lithotripsy was performed exclusively with the Holmium:YAG laser, and all stone fragments were actively extracted and passed off of the surgical field for analysis. Ureteral stents were left in place post-operatively. Stone analysis was performed by microscopic visual inspection, chemical reaction, and/or Fourier transform infrared microspectroscopy.

Results

Twenty-seven patients were identified, with a mean age of 26.8 years (range, 21–34) (Table 1). Analysis found that in 74% of all cases (20 patients) stones were composed predominantly (defined as >50%) of calcium phosphate (hydroxyapatite). In 24% of cases, (7 patients) the stones were composed predominantly of calcium oxalate. The percentages of each stone comprised of different constituents are presented in Table 1. Ten women harbored right sided calculi only, fifteen women harbored left sided calculi only, and two women harbored bilateral calculi. Mean stone size was 5.3 mm (range, 2–11). Stones were removed in the first, second, third trimester and immediately post-partum

Table 1 Patient and stone characteristics

Age (years)	Weeks pregnant at stone removal	Stone size (mm)	Stone composition
21	8	2	28% COM 72% COD
27	15	5	100% CaP
34	18	5	43% CaP 57% COM
30	18	3	100% CaP
23	19	5	67% CaP 20% COM 13% COD
31	20	10	10% CaP 55% COM 35% COD
27	20	N/A	5% CaP 85% COM 10% COD
30	24	4	100% CaP
22	25	4	94% CaP 6% COM
38	25	3	100% CaP
22	28	3	100% CaP
27	27	6	100% CaP
27	27	11	34% CaP 66% COD
25	28	7	55% CaP 5% COM 20% Struvite 20% Organic
26	32	4	41% CaP 59% COM
23	32	2	100% CaP
27	26	6	85% CaP 10% COM 5% COD
29	30	8	82% CaP 15% COM 3% COD
32	25	6	100% CaP
28	18	5	100% CaP
26	35	4	66% CaP 34% COD
20	4 weeks post-partum	7	55% CaP 45% COM
28	4 weeks post-partum	10	82% CaP 15% COM 3% COD
32	6 weeks post-partum	4	100% CaP
26	8 weeks post-partum	5	100% CaP
26	10 weeks post-partum	3	32% CaP 68% COM
26	10 weeks post-partum	6	100% CaP

CaP Calcium Phosphate (hydroxyapatite), *COM* Calcium oxalate monohydrate, *COD* Calcium oxalate dehydrate

in 4, 52, 22, and 22% respectively. Stone removal was performed without complication in all cases.

Twenty patients (74%) had no history of prior stone formation. Seven patients (26%) had previously formed stones, although none of these patients had a known kidney stone at the time they became pregnant (Table 2). Of the women who had previously formed stones, three patients had previously formed predominantly calcium phosphate stones and four patients had previously formed predominantly calcium oxalate stones. Six of the women had previously formed one stone, whereas one woman had formed three prior stones, all of which were composed of predominantly calcium oxalate.

Discussion

Calcium oxalate calculi are the most commonly occurring urinary calculi among all stone formers, accounting for up to 65% of all stones. However, the composition of renal calculi varies with both age and sex, and for men and women of certain age ranges different types of stones predominate. For example, calcium phosphate calculi are more commonly encountered in women of a childbearing age than in women of a more advanced age or among men of any age. Costa-Bauza and colleagues reported that among women 10–35 years of age, 22% of stones are calcium phosphate, a greater percentage than that encountered in women greater than 36 years of age [5]. However, calcium oxalate stones are still the most commonly encountered type of stone in this population, accounting for 42% of all calculi among women 10–35 years of age. Gault and Chafe similarly found that calcium phosphate stones were most commonly found among women between 20 and 39 years of age, although, again, calcium oxalate stones are the most prevalent overall stone type in this age range [6]. Parks and associates, too, have observed that females predominate among calcium phosphate stone formers, although calcium oxalate stones are the most common type of stone among women [7].

Table 2 Patients with prior stone history

Stone composition during pregnancy	Prior stone event 1	Prior stone event 2	Prior stone event 3
43% CaP 57% COM	100% CaP		
67% CaP 20% COM 13% COD	100% CaP		
100% CaP	100% CaP		
66% CaP 34% COD	95% COM 5% COD	1% CaP 76% COM 23% COD	72% COM 28% COD
82% CaP 15% COM 3% COD	100% COM		
100% CaP	42% CaP 58% COD		
100% CaP	95% COM 5% COD		

It is not clear why these studies have demonstrated a greater prevalence of calcium phosphate calculi among young, non-pregnant women than among other populations [5, 6]. However, the prevalence of calcium phosphate stones among pregnant which we observed, 70%, far exceeds even that encountered in a non-pregnant population of a comparable age. Others have noted that the rate of calcium phosphate stone disease may be increasing. Parks and associates reported that the proportion of calcium phosphate in stones has risen over a three decade time period, the reason for which is not clear [7]. An association between the rate of SWL treatments and calcium phosphate stones was also noted, and the authors offered a conjecture that SWL could cause local renal effects which may promote calcium phosphate stone formation. Our study population was naïve to SWL, suggesting that such an effect is not relevant to our present data. Mandel and associates, too, noted an increasing rate of calcium phosphate stones, although the population these authors studied was comprised of a Veterans Administration health system, a disparate population from the cohort of pregnant women presented herein [8].

Calcium phosphate stones are commonly associated with an increased urinary pH. Sefa and associates performed 24 h urine chemistries for pregnant women, and found that in the second trimester of pregnancy urinary pH was significantly higher (6.16) than at any other point during pregnancy or in the post-partum period [9]. These authors also found that urine calcium is significantly higher in the second and third trimesters than in the post-partum period or the first trimester, a finding that has also been reported by others [4, 10, 11]. Maikranz and associates reported that as a result of the hypercalciuria and elevated urinary pH that occurs during pregnancy, calcium phosphate supersaturation increases [12]. Such changes may promote calcium phosphate stone formation, although Maikranz and associates also found that calcium oxalate supersaturation increased; however, the cohort of women in this study were not stone formers, a potential confounding factor that may not allow a perfect extrapolation of these findings to stone forming women.

The composition of renal calculi occurring during pregnancy has not been previously well characterized. Cass and associates reported on a series of pregnant women with stones treated between 1974 and 1984, and found that of 15 stones analyzed, 7 were composed of a calcium carbonate/

calcium phosphate mix, 5 were composed of a calcium phosphate/calcium oxalate mix, and the remainder consisted of 2 uric acid stones and 1 calcium carbonate stone [13]. Horowitz and Schmidt reported that the stones retrieved from 3 pregnant women were composed of calcium oxalate in 2 cases and calcium phosphate in 1 case [14]. Coe and associates reported on women from their stone clinic who became pregnant, but did not specifically address the composition of the stone formed or treated during pregnancy [15].

A kidney stone during pregnancy can be dangerous, not just for the mother, but also for the fetus, as renal colic is associated with pre-term labor and other peri-partum complications [3]. Therefore, insights into the pathogenesis of stone disease during pregnancy are welcome, as they may be formative for future efforts to attenuate this process. We can only speculate on the explanation for the unusual preponderance of calcium phosphate stones in pregnant women, although there may be a transient alteration in urinary pH or urinary calcium that occurs during pregnancy which may promote calcium phosphate stone formation.

Conclusion

Kidney stone disease is a potentially serious complication of pregnancy. What we present in this study is the characterization of kidney stones that are detected in the course of pregnancy, a comprehensive analysis that has not been previously available. These data suggest that these pregnancy-related stones are most commonly composed of calcium phosphate. For reasons that are not clear at this time, it is the minority of stones in this population that are composed of calcium oxalate, which is different than similar cohorts of non-pregnant women who more commonly form calcium oxalate stones. Presumably physiologic alterations that are inherent in the condition of pregnancy may be influential in this phenomenon, although further studies are required to better define this hypothesis.

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