

# Effect of Ramadan Fasting on Urinary Risk Factors for Calculus Formation

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**Introduction.** Even though dehydration could aggravate formation of urinary calculi, the effects of fluid and food restriction on calculus formation is not thoroughly defined. The purpose of this study is to evaluate the effects of fluid and food restriction in Ramadan fasting on urinary factors in kidney and urinary calculus formation. **Materials and Methods.** Fifty-seven men aged 30 to 55 years old, including 37 recurrent calcium calculus formers and 20 with no history of kidney calculi were evaluated for blood tests, ultrasonography investigations, urinalysis, urine culture, and also 24-hour urine collection test. Urinary metabolites including calcium, oxalate, citrate, uric acid, magnesium, phosphate, potassium, sodium, and creatinine were measured before and during Ramadan fasting. The values of calculus-precipitating solutes as well as inhibitory factors were documented thoroughly.

**Results.** Total excretion of calcium, phosphate, and magnesium in 24-hour urine and also urine volume during fasting were significantly lower than those in the nonfasting period. Urine concentration of calcium during fasting was significantly lower than nonfasting ( $P < .001$ ). Urine concentrations of uric acid, citrate, phosphate, sodium, and potassium during fasting were significantly higher than nonfasting. Uric acid supersaturation was accentuated, and calcium phosphate supersaturation was decreased significantly during fasting. There was no significant increase in calcium oxalate supersaturation during the fasting period.

**Conclusions.** Fasting during Ramadan has different effects on total excretion and concentrations of urinary precipitate and inhibitory factors contributing to calculus formation. We did not find enough evidence in favor of increased risks of calculus formation during Ramadan fasting.

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## INTRODUCTION

Urinary calculus formation is a common troublesome and costly urinary system disorder. Even though dehydration could aggravate the process of calculus formation throughout the kidney and urinary outgoing system, the effect of total abstinence from food and water during the month

of Ramadan is unclear. Every year during Ramadan month, fasting is practiced by Muslims throughout the world. During Ramadan, the osmolarity of the urine samples collected, especially in the afternoon become very high (mean, 849 mOsm/kg to 937 mOsm/kg).<sup>1</sup> Not only is the eating pattern greatly altered during the Ramadan period, but also the

amount and type of food eaten during the night may also be significantly different to that usually consumed during the rest of the year. Moreover, there is dehydration during the daylight hours of Ramadan fasting; thus, it seems to be intermittent dehydration.<sup>2</sup>

To date, only limited studies have been conducted about the effect of Ramadan fasting on urinary calculus formation. This study was designed to evaluate the effects of fasting during Ramadan on urinary precipitating and inhibitory factors of calculus formation.

### MATERIALS AND METHODS

We evaluated 57 men aged 30 to 55 years old. They included 37 recurrent calcium calculus formers (based on history, radiologic studies, and calculus analysis) who were recruited from the Stone Clinic of the Urology and Nephrology Research Center of Shahid Beheshti University of Medical Sciences in Tehran. They volunteered for this study and practiced the Ramadan fasting. Also, 20 randomly selected men with no history of kidney disease or calculus formation confirmed by ultrasonography and laboratory tests were included as controls. All participants signed an informed consent form for their participation. None of the participant had any established metabolic, gastrointestinal, liver, kidney, cardiovascular, or endocrine disorders except for urinary calculus formation in the calculus former group. Individuals with urinary tract anomalies, urinary tract infection, obesity (body mass index > 30 kg/m<sup>2</sup>), and those who were taking medicines that could affect calcium metabolism and other urinary factors were excluded from the study.

Twenty-four-hour urine samples were collected before the start of Ramadan fasting (U3) and during Ramadan fasting. Fasting was between 4:00 and 19:00 (15 hours). Collection of the 24-hour urine during Ramadan fasting was divided in 2 periods and urine was collected in 2 containers. In the first one, urine was collected for 20 hours (19:00 to 15:00 of the following day) (U1), and in the second one urine was collected for 4 hours (15:00 to 19:00) that contained a concentrated urine (U2).

All subjects underwent blood tests including complete blood count, blood urea nitrogen, serum creatinine, serum sodium, serum potassium, fasting blood glucose, serum calcium, serum

phosphate, serum alkaline phosphatase, serum parathyroid hormone, serum uric acid, and urine analysis and urine culture. Twenty-four-hour urine samples were collected in polyethylene containers with hydrochloric acid 6N or boric acid as preservative and were stored at -20°C and analyzed within a month. For metabolic evaluation, urine parameters such as volume, specific gravity, creatinine, phosphate, calcium, oxalate, citrate, sodium, potassium, magnesium, uric acid, pH (in fresh urine), urinary supersaturation of calcium oxalate, calcium phosphate, and uric acid were measured using standard methods as follows: sodium (flame photometry; coefficient of variation [CV], 1.9%), potassium (flame photometry; CV, 1.5%), pH (reflectance photometry), specific gravity (refractometry), protein (sulfosalicylic acid, quantitative; CV, 2.1%), creatinine (Jaffe kinetic; CV, 1.8%), calcium (Arsenazo, colorimetric; CV, 2.4%), oxalate (enzymatic colorimetric, LTA, Milano, Italy; CV, 3.57%), uric acid (enzymatic uricase; CV, 4.2%), citrate (enzymatic colorimetric, LTA, Milano, Italy; CV, 3.18%), magnesium (colorimetric, calmagite; CV, 2.9%), and inorganic phosphate (phosphomolybdate; CV, 2.5%). The Lithorisk software (Biohealth, Turin, Italy) was utilized to calculate the supersaturation.

The data was analyzed using the SPSS software (Statistical Package for the Social Sciences, version 17.0, SPSS Inc, Chicago, Ill, USA). Quantitative variables were expressed as mean ± standard deviation. The three urine collections were compared for urine concentrations and supersaturations and the 24-hour urine collection during fasting (U1 + U<sub>2</sub>) was compared with that of nonfasting period (U3) using the paired *t* test. A *P* value less than .05 was considered significant.

### RESULTS

The mean age of the participants was 41.66 ± 6.80 years. Urine concentration of calcium during fasting (8.05 ± 4.46 mg/dL) was significantly lower than the nonfasting period concentration (14.59 ± 6.38 mg/dL; *P* < .001). In contrast, urine concentrations of uric acid, citrate, phosphate, sodium, and potassium during fasting were significantly higher than those during the nonfasting period (Table 1). These changes were the same in both calculus formers and control groups (serum sodium level was significantly lower during fasting in the

calculus former group; Tables 2 and 3).

Total excretion of calcium ( $144.89 \pm 65.89$  mg/dL versus  $232.00 \pm 114.31$  mg/dL), phosphate,

and magnesium, and also urine volume during fasting were significantly lower than those of the nonfasting, and total excretion of uric acid, oxalate,

**Table 1.** Urine Metabolite Concentrations and Supersaturations During Fasting and Nonfasting Periods in Recurrent Calcium Calculus Formers and Healthy Controls (n = 57)

Parameter	Urine Sample			P		
	Nonconcentrated Fasting (U1)	Concentrated Fasting (U2)	Nonfasting (U3)	U1, U2	U1, U3	U2, U3
Calcium, mg/dL	11.41 ± 6.19	8.05 ± 4.46	14.59 ± 6.38	< .001	.004	< .001
Oxalate, mg/dL	3.01 ± 1.76	3.02 ± 1.65	2.63 ± 0.73	.99	.14	.12
Uric acid, mg/dL	27.46 ± 15.72	50.81 ± 26.34	26.03 ± 13.11	< .001	.60	< .001
Citrate, mg/dL	52.10 ± 59.15	60.14 ± 67.37	37.52 ± 27.82	.37	.13	.027
Phosphate, mg/dL	48.39 ± 24.94	103.39 ± 128.23	56.87 ± 22.59	.002	.031	.008
Magnesium, mg/dL	6.873 ± 5.464	7.190 ± 11.422	6.637 ± 2.465	.85	.73	.73
Potassium, mEq/dL	3.43 ± 1.78	8.23 ± 4.46	3.71 ± 1.49	< .001	.26	< .001
Sodium, mEq/dL	12.00 ± 5.55	16.92 ± 8.28	11.81 ± 4.66	< .001	.82	< .001
Calcium oxalate supersaturation	5.755 ± 2.673	6.752 ± 5.113	8.308 ± 4.554	.17	.003	.07
Calcium Phosphate supersaturation	0.626 ± 1.535	0.294 ± 0.961	0.786 ± 1.175	.10	.54	.01
Uric acid supersaturation	1.259 ± 0.921	2.836 ± 2.209	1.292 ± 0.810	< .001	.85	< .001

**Table 2.** Urine Metabolite Concentrations and Supersaturations During Fasting and Nonfasting Periods in Recurrent Calcium Calculus Formers (n = 37)

Parameter	Urine Sample			P		
	Nonconcentrated Fasting (U1)	Concentrated Fasting (U2)	Nonfasting (U3)	U1, U2	U1, U3	U2, U3
Calcium, mg/dL	10.69 ± 5.44	8.09 ± 4.38	15.21 ± 7.13	.02	.002	< .001
Oxalate, mg/dL	3.04 ± 1.92	2.79 ± 1.50	2.62 ± 0.62	.49	.18	.54
Uric acid, mg/dL	25.30 ± 16.20	49.20 ± 28.97	26.18 ± 12.64	< .001	.81	< .001
Citrate, mg/dL	53.18 ± 67.00	52.59 ± 57.58	36.96 ± 30.55	.96	.25	.19
Phosphate, mg/dL	44.84 ± 20.50	111.10 ± 152.88	52.80 ± 21.66	.02	.04	.03
Magnesium, mg/dL	6.187 ± 5.548	7.726 ± 14.127	6.232 ± 2.363	.54	.96	.50
Potassium, mEq/dL	3.06 ± 1.63	9.97 ± 11.95	3.56 ± 1.53	< .001	.11	< .001
Sodium, mEq/dL	10.94 ± 5.64	8.09 ± 3.56	10.57 ± 3.56	< .001	.72	< .001
Calcium oxalate supersaturation	6.247 ± 4.513	6.537 ± 4.616	9.343 ± 4.957	.68	.008	.009
Calcium Phosphate supersaturation	0.504 ± 0.905	0.408 ± 1.179	0.780 ± 1.295	.47	.29	.17
Uric acid supersaturation	1.115 ± 0.688	2.668 ± 2.468	1.436 ± 0.906	< .001	.10	.006

**Table 3.** Urine Metabolite Concentrations and Supersaturations During Fasting and Nonfasting Periods in Healthy Controls With No History of Urinary Calculi (n = 20)

Parameter	Urine Sample			P		
	Nonconcentrated Fasting (U1)	Concentrated Fasting (U2)	Nonfasting (U3)	U1, U2	U1, U3	U2, U3
Calcium, mg/dL	12.74 ± 7.37	7.99 ± 4.71	13.45 ± 4.67	.02	.68	.001
Oxalate, mg/dL	2.93 ± 1.50	3.41 ± 1.86	2.64 ± 0.89	.40	.53	.12
Uric acid, mg/dL	31.44 ± 14.32	53.76 ± 20.97	25.76 ± 14.29	< .001	.15	< .001
Citrate, mg/dL	50.10 ± 42.45	74.10 ± 82.34	38.53 ± 22.59	.15	.22	.07
Phosphate, mg/dL	54.96 ± 31.09	89.15 ± 62.04	64.39 ± 22.87	.02	.29	.05
Magnesium, mg/dL	8.143 ± 5.201	6.200 ± 2.191	7.388 ± 2.533	.07	.50	.02
Potassium, mEq/dL	4.10 ± 1.91	8.49 ± 5.86	3.96 ± 1.41	.002	.74	.002
Sodium, mEq/dL	13.96 ± 4.93	18.49 ± 11.30	14.09 ± 5.61	.07	.93	.06
Calcium oxalate supersaturation	4.847 ± 2.673	7.149 ± 6.036	6.393 ± 2.937	.16	.17	.60
Calcium Phosphate supersaturation	0.851 ± 2.305	0.083 ± 0.108	0.796 ± 0.941	.15	.92	.004
Uric acid supersaturation	1.526 ± 1.219	3.147 ± 1.637	1.024 ± 0.511	< .001	.14	< .001

**Table 4.** Twenty-Four-Hour Urine Metabolites Concentrations During Fasting and Nonfasting Periods in Recurrent Calculus Formers and Healthy Controls (n = 57)

Parameter	Nonfasting	Fasting	P
Calcium, mg/dL	232.00 ± 114.31	144.89 ± 65.89	< .001
Oxalate, mg/dL	43.16 ± 15.47	40.70 ± 19.80	.36
Uric acid, mg/dL	422.00 ± 226.55	440.48 ± 210.71	.66
Citrate, mg/dL	593.72 ± 456.11	738.35 ± 756.43	.28
Phosphate, mg/dL	903.21 ± 398.36	746.12 ± 234.45	.01
Magnesium, mg/dL	105.596 ± 40.123	88.374 ± 46.534	.02
Potassium, mEq/dL	58.86 ± 24.10	57.79 ± 22.76	.79
Sodium, mEq/dL	188.11 ± 75.61	178.40 ± 77.23	.42
Urine volume, mL/d	1645.08 ± 429.12	1484.29 ± 546.68	< .001

**Table 5.** Twenty-Four-Hour Urine Metabolites Concentrations During Fasting and Nonfasting Periods in Recurrent Calculus Formers (n = 37)

Parameter	Nonfasting	Fasting	P
Calcium, mg/dL	253.03 ± 130.53	147.03 ± 63.37	< .001
Oxalate, mg/dL	45.27 ± 15.20	43.56 ± 23.01	.64
Uric acid, mg/dL	455.24 ± 245.69	419.07 ± 211.32	.52
Citrate, mg/dL	627.75 ± 533.97	797.70 ± 874.13	.39
Phosphate, mg/dL	884.90 ± 425.14	747.91 ± 200.51	.08
Magnesium, mg/dL	104.68 ± 42.44	84.40 ± 39.49	.02
Potassium, mEq/dL	60.43 ± 27.46	55.55 ± 19.71	.36
Sodium, mEq/dL	179.08 ± 71.98	169.64 ± 68.39	.54
Urine volume, mL/d	1736.76 ± 465.55	1583.92 ± 575.90	.001

**Table 6.** Twenty-Four-Hour Urine Metabolites Concentrations During Fasting and Nonfasting Periods in Healthy Controls With No History of Urinary Calculus (n = 20)

Parameter	Nonfasting	Fasting	P
Calcium, mg/dL	193.10 ± 61.45	140.93 ± 71.84	.01
Oxalate, mg/dL	39.27 ± 15.61	35.40 ± 10.34	.34
Uric acid, mg/dL	360.50 ± 175.41	480.10 ± 209.05	.047
Citrate, mg/dL	530.75 ± 257.81	628.55 ± 468.14	.42
Phosphate, mg/dL	937.03 ± 351.27	742.81 ± 292.95	.050
Magnesium, mg/dL	107.30 ± 36.42	95.73 ± 57.79	.37
Potassium, mEq/dL	55.95 ± 16.43	61.95 ± 27.62	.32
Sodium, mEq/dL	204.80 ± 81.12	194.60 ± 91.07	.60
Urine volume, mL/d	1475.50 ± 292.28	1300.00 ± 444.26	.002

citrate, sodium, and potassium during fasting were not significantly different than those of the nonfasting (Tables 4 to 6).

Uric acid supersaturation increased and calcium phosphate supersaturation decreased significantly during fasting. Calcium oxalate supersaturation did not increase during fasting, and even in the recurrent calculus former group, it showed a decrease (Tables 1 to 3).

## DISCUSSION

Our findings showed that calcium concentration and the total amount of calcium, phosphate,

magnesium, and urine volume during fasting are significantly less than those during the nonfasting period. Also, concentrations of uric acid, citrate, phosphate, sodium, and potassium were significantly higher during fasting. Uric acid supersaturation increased during fasting, while calcium phosphate supersaturation decreased. On the other hand, calcium oxalate supersaturation was not significantly higher, and even it decreased, during fasting.

In our study, there were some changes in excretion of various urinary lithogenic and inhibitory substances during fasting. Some changes

in favor of decreased lithogenesis included decreased urine calcium concentration and total calcium and phosphate excretion, increased citrate and potassium concentration, and decreased supersaturation of calcium phosphate (and even calcium oxalate). Some other changes were in favor of increased lithogenesis, which were increased uric acid, phosphate, and sodium concentrations; and increased uric acid supersaturation, and decreased urine volume and magnesium excretion during fasting.

Reports on urinary factors associated with fasting are scarce. In one study, the prevalence of renal colic in Ramadan was compared with other months of the lunar year in 574 participants who were admitted to 2 medical centers in Iran.<sup>3</sup> Colic episodes were more common in June, July, and November. Forty-three patients with renal colic were admitted in Ramadan. The frequency of renal colic cases in Ramadan was not significantly different from the mean admissions of the year (48 patients). There was also no significant difference between the frequency of admissions in Ramadan and the mean admissions during the cold half of the year (37 patients). Furthermore, the mean admissions in warm seasons (64 patients) were significantly higher than that in Ramadan ( $P < .001$ ).<sup>3</sup> According to the study of Al-Hadramy, there is a steady increase in urinary calculus colic in the hot seasons with a maximum rate in the months of June, July, and August and the month in which renal colic episodes are lowest is March.<sup>4</sup> This report showed a strong correlation between renal colic and both temperature and atmospheric pressure ( $P < .001$ ). No significant increase in urinary renal colic was observed in relation to Ramadan fasting or the pilgrimage festival.<sup>4</sup>

According to the above studies, there are correlations between the occurrence of urinary renal colic and the hot seasons but not with Ramadan. In our study, Ramadan fasting has conflicting effects on calculus formation factors, and we did not find enough evidence in favor of increased calculus formation risks. Findings of studies on renal colic in Ramadan by Basiri and colleagues and al-Hadramy seem to be compatible with our study,<sup>3,4</sup> but we have to consider that calculus formation takes time and decreased urinary renal colic does not necessarily mean a decrease in calculus formation.

Zghal and colleagues<sup>5</sup> evaluated the effect of fluid and diet restriction in fasting on the biochemical factors of calculus formation. The study included 90 patients divided in 3 groups of healthy fasting individuals, healthy nonfasting individuals, and nonfasting patients with calcium lithiasis. Supersaturation of urine with oxalate, uric acid, and brushite were the same for healthy fasting individuals and the patients and higher than that for nonfasting participants. Crystalluria was predominant in patients with lithiasis compared with healthy nonfasting individuals (58% versus 11.4%). Oxalate monohydrate (whewellite) and uric crystal did not exist in the healthy nonfasting people, but reached 4% and 12%, respectively, in the fasting participants and lithiasis patients. The crystalluria profile was the same in the healthy fasting participants and calcium lithiasis patients.<sup>5</sup> In this study, comparison was between the three groups. We compared these factors within each group during fasting and nonfasting periods. Supersaturation of oxalate, uric acid, and brushite in this study were the same in healthy fasting participants and nonfasting individuals with calcium lithiasis, but in our study, supersaturation of uric acid in the healthy fasting group was higher than nonfasting patients with calcium lithiasis. However, supersaturation of brushite and calcium oxalate was less than that in nonfasting individuals with the history of calcium lithiasis.

In 20 Malaysian Muslims urine was collected before, during, and after Ramadan fasting each in the morning (8:00 to 12:00), afternoon (12:00 to 16:00), and overnight (16:00 to 08:00).<sup>6</sup> The 24-hour urine output during Ramadan tended to be lower than that of the prefasting level; however, the decline was not significant. The total 24-hour sodium output declined significantly throughout the fasting period. There was some decline in potassium output, but this was less dramatic compared with the sodium output. The concentrations of sodium and potassium were not consistently increased during Ramadan, even during the morning and afternoon when urine volumes tended to be decreased, and mostly were maintained near or even below prefasting levels.<sup>6</sup>

In the Gubbio Population Study in north central Italy about the effect of urinary sodium-potassium ratio on calculus formation,<sup>7</sup> compared to healthy individuals, calculus formers had higher urinary



sodium-potassium ratio ( $P < .01$ ). Based on these observations, it can be hypothesized that individuals with high urinary sodium-potassium ratio are at a higher risk of urinary calculus disease.<sup>7</sup> In our study, concentrations of sodium and potassium were significantly increased during fasting, of which potassium concentration increment was dominant. Total sodium and potassium excretions were not significantly different during fasting. Urine volume significantly decreased during fasting.

### CONCLUSIONS

Ramadan fasting causes some changes in urinary metabolites that have different effects on calculus formation. There is not enough evidence that Ramadan fasting increases urinary calculus formation, but the effect of fasting on calculus formation risk factors and epidemiology of urolithiasis need to be investigated by further studies.

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### CONFLICT OF INTEREST

None declared.

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