

מעבדה מטבולית

טלפון: 2553/7068-530-03 פקס: 2552-530-03

ClinicalBiochemistryLab@sheba.gov.il

Citrate Determination in 24-Hour Urine Collection, Quantitative LC-MS/MS

Useful For:

1. Evaluating urinary citrate levels to assess risk factors for kidney stone formation.
2. Monitoring treatment to prevent recurrence of calcium-containing kidney stones.
3. Diagnosing metabolic disorders related to citrate abnormalities, such as renal tubular acidosis.

Methodology:

Quantitative analysis is performed using liquid chromatography tandem mass spectrometry (LC-MS/MS) with Electrospray Ionization (ESI) technique.

Clinical Information:

Kidney stone disease is the most common chronic kidney condition and has been increasingly linked to systemic conditions. Overweight, hypertension and diabetes have all been shown to be associated with an increased risk of kidney stone disease. Urinary citrate plays a protective role against stone formation by inhibiting calcium crystallization and aggregation. Low urinary citrate (hypocitraturia) is a significant risk factor for nephrolithiasis, particularly calcium-containing stones, as it reduces the ability to prevent calcium precipitation. Citrate acts as a natural chelator by binding to calcium and forming soluble complexes.

Decreased urinary citrate concentration may occur due to various conditions:

- **Disturbances of acid-base balance:** Patients with metabolic acidosis, including distal renal tubular acidosis, can have increased citrate reabsorption in renal tubules, leading to hypocitraturia.
- **Dietary factors:** High protein intake or low fruit and vegetable consumption can decrease urinary citrate levels.
- **Medications:** Certain diuretics, such as acetazolamide or thiazide diuretics, may reduce urinary citrate.
- **Chronic kidney disease or chronic diarrhea:** These can lead to imbalances in acid-base homeostasis, resulting in low citrate excretion.

Testing urinary citrate levels in a 24-hour collection is essential for comprehensive metabolic evaluation in patients with kidney stones. This testing is strongly recommended by multiple

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published guidelines, including the American Urological Association. The 24-hour urine collection provides a complete picture of the patient's urinary citrate excretion over an entire day, accounting for fluctuations due to: dietary intake (e.g., citrate-rich foods such as fruits and vegetables), circadian rhythms affecting renal excretion and variable hydration levels during the day. A random urine sample only reflects citrate excretion at a single point in time and may fail to capture daily variations. This can lead to false-normal or false-elevated results, making it unreliable for accurately diagnosing citrate abnormalities. In young children until 16 years of age, a random urine sample can be assayed for urine citrate: creatinine ratio.

Hypocitraturia is often treatable, and therapies involving dietary changes, citrate supplementation, or alkali therapy (such as potassium citrate) can help reduce stone formation risk. Additionally, elevated urinary citrate levels are rare but may occasionally indicate systemic metabolic abnormalities or excessive alkali therapy.

Necessary Information:

- 24-hour urine volume (in milliliters)
- Completed test order form
- Clinical background and suspected conditions (e.g., stone history, renal tubular acidosis)
- Payment documentation

Deliver samples cold or frozen to the Mega-Lab laboratory, ground floor, weekdays between 08:00-15:00.

Collection Instructions:

1. Add 30 mL of 6M HCl as a preservative at the start of collection and refrigerate the specimen during and after collection. Use clean plastic containers with plastic caps (no metal caps).
2. Collect urine over a 24-hour period.
3. Urine pH should be maintained between 1 and 4 to prevent degradation.
4. The patient's first morning urine is not to be collected. Then collect all urine including the next morning first urine in a collection container containing the preservative 6 M HCl. 24-hour collection period in total.

Patient Preparation:

Avoid citrus fruits, vitamin C supplements (>2g/day), and vitamin C-rich foods (such as oranges, tomatoes, peppers, broccoli) for 48 hours before collection, as these may alter citrate levels.

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Specimen Volume:

Preferred volume: 5 mL, Minimum volume: 1 mL

Specimen Stability Information:

- **Frozen (preferred):** Stable for 60 days at -20°C.
- **Refrigerated:** Stable for 29 days.

Interpretation:

- **Low citrate levels (hypocitraturia):** Common in calcium oxalate or calcium phosphate stone formers. Associated with metabolic acidosis, dietary imbalances, renal tubular acidosis, or chronic diarrhea. Management often involves increasing urinary citrate levels through potassium citrate supplementation or dietary modifications.
- **Normal or elevated citrate levels:** Rare but may occasionally be linked to excessive alkali therapy or systemic disorders.

For patients with urolithiasis (kidney stones), optimizing urinary citrate levels may prevent stone recurrence and reduce progression risk.

Clinical Reference Range:

24 hours urine collection

288-903 mg citrate/24 hr

Random urine

age	mg citrate/gr creatinine
<6M	219-3775
6M-3Y	143-2440
3-8Y	255-1711
8-16Y	112-1296

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Turnaround Time:

27 working days

Ministry of Health Code:

882507

References:

1. Christopher J. Corder; Banshi M. Rath; Sairah Sharif; Stephen W. Leslie. *24-Hour Urine Collection*, Last Update: August 14, 2023.
2. Marshall D.J., Adaway J.E., Keevil B.G. A combined liquid chromatography tandem mass spectrometry assay for the quantification of urinary oxalate and citrate in patients with nephrolithiasis. *Ann. Clin. Biochem.* 2018;55:461–468.
3. Pak C.Y. Etiology and treatment of hypocitraturic nephrolithiasis. *Am J Kidney Dis.* 1991;17(4):420–425.
4. Preminger G.M., Curhan G.C., Jungers P., et al. *Nephrolithiasis treatment and management*. *Lancet.* 2004.
5. Pearle MS, Goldfarb DS, Assimos DG, Curhan G, Denu-Ciocca CJ, Matlaga BR, Monga M, Penniston KL, Preminger GM, Turk TM, White JR., American Urological Association. Medical management of kidney stones: AUA guideline. *J Urol.* 2014 Aug;192(2):316-24.