



Discover Fabry Disease

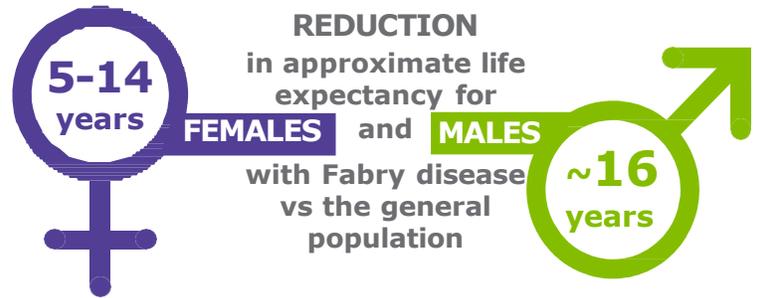
THE ROLE OF THE NEPHROLOGIST

RENAL MANIFESTATIONS OF FABRY DISEASE ARE COMMON AND CAN BE LIFE THREATENING.^{1,2}

Fabry disease is a rare, progressive, and potentially life-threatening disorder that starts in early childhood and affects men and women.²⁻⁴

As an X-linked lysosomal storage disorder that is multisystemic, Fabry disease is caused by complete or partial deficiency of the lysosomal enzyme α -GAL A, leading to GL-3* and lyso-GL-3 accumulation that can result in damage to the kidneys, heart, and cerebrovascular system.⁴

EARLY DIAGNOSIS AND MANAGEMENT ARE CRITICAL AS FABRY DISEASE CAN DECREASE LIFE EXPECTANCY DUE TO ORGAN DAMAGE.⁴⁻⁷



THE PREVALENCE OF FABRY DISEASE IN THE DIALYSIS POPULATION IS HIGHER THAN IN THE GENERAL POPULATION.⁸⁻¹²

10x - 108x higher in **FEMALES**⁸⁻¹⁰

80x - 480x higher in **MALES**⁸⁻¹²

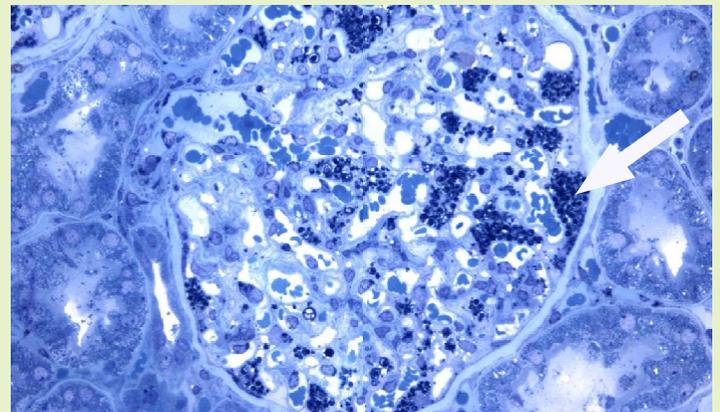
IDENTIFY FREQUENT RENAL SIGNS AND SYMPTOMS OF FABRY DISEASE

Patients may experience a myriad of symptoms, including:

- **Microalbuminuria, Proteinuria**^{1,2}
- **Podocyte injury (can occur in the absence of albuminuria)**^{1,2,13}
- **Elevated serum creatinine**^{1,2}
- **Glomerular sclerosis**^{1,2}
- **Fibrosis**^{1,2}
- **Progressive renal insufficiency/ESRD**^{1,2}
- Progressive LVH, angina, myocardial fibrosis, and arrhythmias^{3,14}
- Early ischemic stroke^{3,14}
- Peripheral neuropathy of extremities/episodic pain crisis beginning in childhood¹⁴
- Hypohydrosis¹⁴
- GI manifestations: diarrhea, abdominal pain¹⁴
- Angiokeratomas¹⁴

RENAL SYMPTOMS OF FABRY DISEASE CAN BE CONFUSED WITH

- Diabetes mellitus, arterial hypertension, or systemic lupus erythematosus¹⁵
- Chronic glomerulonephritis²
- Familial Mediterranean fever and secondary amyloidosis¹⁶



Kidney biopsy (light microscopy): the purple stain is on the podocytes where there is the most prominent collection of GL-3 in the kidney. Reprinted with permission from *Orphanet J Rare Dis*. Germain DP. 2010;5:30.

*GL-3 and Gb3 are interchangeable terms for globotriaosylceramide.

α -GAL A, α -galactosidase A; ESRD, end-stage renal disease; GL-3, globotriaosylceramide; LVH, left ventricular hypertrophy; lyso-GL-3, globotriaosylsphingosine.

RENAL MANIFESTATIONS ARE A PROMINENT INDICATION OF FABRY DISEASE AND CAN BE LIFE THREATENING¹⁷

CONSIDER FABRY DISEASE IN YOUR DIFFERENTIAL DIAGNOSIS WHEN¹⁵:

Presentation

Microalbuminuria, proteinuria, reduced GFR, hematuria (rare), renal cysts (mainly parapelvic), and (in early disease) reduced systemic BP and glomerular hyperfiltration¹⁸

Family History

Cardiomyopathy, arrhythmias, premature stroke, sudden cardiac death, and renal failure^{19,20}

Laboratory and Biopsy Findings

Urinalysis: "Maltese cross," "urinary mulberry cells," biomarkers GL3* and lyso-GL3¹⁸

Biopsy: Glomerulosclerosis, vascular lesions, vacuolation, and lysosomal GL3 deposits¹⁸

Rule out Fabry disease in your patients with unexplained CKD.

RENAL BEST PRACTICE SCREENING RECOMMENDATIONS²¹

TESTING IS STRAIGHTFORWARD^{14,22}

Males



Screening **MALES** <50 years of age with unexplained CKD

Females



Screening **FEMALES** at any age with unexplained CKD and other symptoms associated with Fabry disease

α-GAL A enzyme assay

and/or

GLA gene sequencing

GLA gene sequencing

Affected females may have normal-to-low enzyme activity in plasma or leukocytes; therefore, *GLA* gene sequencing is required to confirm diagnosis in females.

Damage to renal, cardiac, and cerebrovascular systems can have a life-threatening impact. Monitor patients in accordance with published management guidelines and clinicians' medical expertise.¹⁴

Laboratories across the United States offer diagnostic tests for Fabry disease. Visit <https://www.discoverfabry.com/diagnosing-fabry>



*GL-3 and Gb3 are interchangeable terms for globotriaosylceramide. Fabry-specific biomarkers GL-3 and lyso-GL-3 are elevated in urine and plasma in males. Plasma GL3 can be normal in affected females.

BP, blood pressure; CKD, chronic kidney disease; GFR, glomerular filtration rate; *GLA*, galactosidase-alfa.

1. Waldek S, et al. *BMC Nephrol*. 2014;15:72. 2. Germain DP. *Orphanet J Rare Dis*. 2010;5(30):1-49. 3. Azevedo O, et al. *Int J Mol Sci*. 2021;22(9):4434. 4. Lidove O, et al. *Clin Genet*. 2012;81(6):571-577. 5. Mehta A, et al. *J Med Genet* 2009;46:548-552. 6. Arias E, et al. Vital Statistics Rapid Release. 2021. Available at: <https://www.cdc.gov/nchs/data/vsrr/vsrr015-508.pdf>. Accessed November 2021. 7. Waldek S, et al. *Genet Med*. 2009;11(11):790-796. 8. Merta M, et al. *Nephrol Dial Transplant*. 2007;22(1):179-186. 9. Gaspar P, et al. *BMC Med Genet*. 2010;11:19. 10. Linthorst GE, et al. *Nephrol Dial Transplant*. 2003;18(8):1581-1584. 11. Nakao S, et al. *Kidney Int*. 2003;64(3):801-807. 12. Kotanko P, et al. *J Am Soc Nephrol*. 2004;15(5):1323-1329. 13. Tondel C, et al. *Nephron*. 2015;129(1):16-21. 14. Ortiz A, et al. *Mol Genet Metab*. 2018;123(4):416-427. 15. Hoffmann B, et al. *Dtsch Arztebl Int*. 2009;106(26):440-447. 16. Turkmen K, et al. *Kidney Blood Press Res*. 2016;41(6):1016-1024. 17. Schiffmann R, et al. *Kidney Int*. 2017;91(2):284-293. 18. Silva CAB, et al. *Can J Kid Health Dis*. 2021;8:1-14. 19. Baig S, et al. *Europace*. 2018;20(F12):f153-f161. 20. Yousef Z, et al. *Eur Heart J*. 2013;34(11):802-808. 21. Terry W, et al. *Nephrol Dial Transplant*. 2013;28(3):505-517. 22. Biegstraaten M, et al. *Orphanet J Rare Dis*. 2015;10:36.