MAYO CLINIC LABORATORIES

Test Definition: 2HGA

2-Hydroxyglutaric Acid Chiral Analysis, Quantitative, Random, Urine

Overview

Useful For

Determining type of 2-hydroxyglutaric aciduria by chiral analysis of urine

Special Instructions

- Biochemical Genetics Patient Information

Highlights

This test provides differentiation of the 3 subtypes of 2-hydroxyglutaric aciduria: D-2-hydroxyglutaric aciduria, L-2-hydroxyglutaric aciduria, and combined D,L-2-hydroxyglutaric aciduria. It also provides a quantitative result of the D- and L-enantiomers of 2-hydroxyglutaric acid via gas chromatography-mass spectrometry analysis.

Method Name

Gas Chromatography Mass Spectrometry (GC-MS)

NY State Available

Yes

Specimen

Specimen Type

Urine

Necessary Information

1. Age and sex of patient are required.

2. Biochemical Genetics Patient Information (T602) is recommended, but not required, to be filled out and sent with the specimen to aid in the interpretation of test results.

Specimen Required

Supplies: Urine Tube, 10 mL (T068)

Container/Tube: Plastic, 10-mL urine tube

Specimen Volume: 10 mL

Pediatric: If the collection volume appears insufficient, submit as much specimen as possible in a single container; the laboratory will determine if volume is sufficient for test.

Collection Instructions:

1. Collect a random urine specimen (first morning void preferred)
2. No preservative

Forms

1. Biochemical Genetics Patient Information (T602)
2. If not ordering electronically, complete, print, and send a Biochemical Genetics Test Request (T798) with the specimen.

Specimen Minimum Volume
1 mL

Reject Due To

All specimens will be evaluated at Mayo Clinic Laboratories for test suitability.

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Urine	Frozen (preferred)	416 days	
	Ambient	14 days	
	Refrigerated	14 days	

Clinical & Interpretive

Clinical Information
2-hydroxyglutaric aciduria disorders are a group of cerebral organic acidurias that present biochemically with an elevation of 2-hydroxyglutaric acid (2-HGA) in the urine. There are 2 enantiomers of 2-HGA, the D-form and the L-form. Depending on the genetic defect, individuals may have an elevation of one or both forms of 2-HGA. Routine organic acid analysis (OAU / Organic Acids Screen, Random, Urine), while able to detect 2-HGA, is unable to distinguish between the 2 enantiomers; however, they can be separated with this more specialized biochemical test.

L-2-hydroxyglutaric aciduria (L-2-HGA) is an autosomal recessive disorder caused by disease-causing variants in the *L2HGDH* gene. This disorder is characterized by progressive cerebellar ataxia and intellectual disability, seizures, and macrocephaly beginning in infancy or early childhood. Symptoms worsen over time, leading to severe disability by early adulthood. Magnetic resonance imaging findings include subcortical leukoencephalopathy, generalized cerebellar and cerebral atrophy, and atrophy of the corpus callosum.

D-2-hydroxylglutaric aciduria (D-2-HGA) is characterized by elevated levels of D-2-hydroxyglutaric acid (D-2-HG) and typically manifest clinically with developmental delay, seizures, and hypotonia, though can vary widely from asymptomatic to severe. There are 2 types of D-2-HGA depending on the genetic cause. D-2-HGA can either be autosomal recessive due to disease-causing variants in *D2HGDH* results in reduced enzymatic activity (type I), or autosomal dominant, with gain-of-function variants in *IDH2* causing overproduction of D-2-HG (type II).

Combined D,L-2-hydroxylglutaric aciduria (D,L-2-HGA) is the most severe of the 3 types and is caused by defects in *SLC25A1*, which encodes the mitochondrial citrate carrier. It is characterized by neonatal-onset encephalopathy with severe muscular weakness, intractable seizures, respiratory distress, and lack of psychomotor development resulting in early death.

Molecular genetic testing is available (2OHGP / 2-Hydroxyglutaric Aciduria Gene Panel, Varies), which includes analysis of *D2HGDH*, *L2HGDH*, *IDH2*, and *SLC25A1* and can be used to confirm abnormal urine results.

Reference Values

Age	D-2-hydroxyglutaric acid (mmol/mol creatinine)	L-2-hydroxyglutaric acid (mmol/mol creatinine)
0-11 months	< or =14.11	< or =17.38
12-23 months	< or =13.76	< or =17.03
24-35 months	< or =13.38	< or =16.63
3 years	< or =12.96	< or =16.18
4 years	< or =12.20	< or =15.35
5 years	< or =11.40	< or =14.44
6 years	< or =10.56	< or =13.46
7 years	< or =9.71	< or =12.43
8 years	< or =8.93	< or =11.44
9 years	< or =8.21	< or =10.50
10 years	< or =7.56	< or =9.66
11 years	< or =6.99	< or =8.94
12 years	< or =6.47	< or =8.33
13 years	< or =6.01	< or =7.83
14 years	< or =5.60	< or =7.44
15 years	< or =5.23	< or =7.14
16 years	< or =4.91	< or =6.93
17 years	< or =4.63	< or =6.78
18 years	< or =4.40	< or =6.69
19 years	< or =4.21	< or =6.63
20 years	< or =4.07	< or =6.60
21 years	< or =3.96	< or =6.59
22 years	< or =3.88	< or =6.58
23 years	< or =3.81	< or =6.56
24 years	< or =3.76	< or =6.54
25 years	< or =3.71	< or =6.50
26 years	< or =3.67	< or =6.44
27 years	< or =3.63	< or =6.37
28 years	< or =3.59	< or =6.27
29 years	< or =3.56	< or =6.15
30 years	< or =3.54	< or =6.02
31 years	< or =3.52	< or =5.87
32 years	< or =3.50	< or =5.72
33 years	< or =3.49	< or =5.57
34 years	< or =3.48	< or =5.41

35 years	< or =3.46	< or =5.26
36 years	< or =3.45	< or =5.13
37 years	< or =3.43	< or =5.00
38 years	< or =3.42	< or =4.88
39 years	< or =3.40	< or =4.78
40 years	< or =3.39	< or =4.70
41 years	< or =3.37	< or =4.62
42 years	< or =3.35	< or =4.55
43 years	< or =3.33	< or =4.50
44 years	< or =3.30	< or =4.44
45 years	< or =3.28	< or =4.40
46 years	< or =3.24	< or =4.35
47 years	< or =3.21	< or =4.31
48 years	< or =3.17	< or =4.27
49 years	< or =3.13	< or =4.23
50 years	< or =3.10	< or =4.19
51 years	< or =3.07	< or =4.16
52 years	< or =3.04	< or =4.12
53 years	< or =3.01	< or =4.10
54 years	< or =2.99	< or =4.07
55 years	< or =2.97	< or =4.04
56 years	< or =2.95	< or =4.01
57 years	< or =2.93	< or =3.98
58 years	< or =2.91	< or =3.94
59 years	< or =2.89	< or =3.91
60 years	< or =2.87	< or =3.87
61 years	< or =2.85	< or =3.84
62 years	< or =2.83	< or =3.80
63 years	< or =2.79	< or =3.78
64 years	< or =2.76	< or =3.75
65 years	< or =2.71	< or =3.73
66 years	< or =2.67	< or =3.72
67 years	< or =2.61	< or =3.71
68 years	< or =2.56	< or =3.69
69 years	< or =2.50	< or =3.68
70 years	< or =2.44	< or =3.66
71 years	< or =2.38	< or =3.64
72 years	< or =2.32	< or =3.61
73 years	< or =2.26	< or =3.56
74 years	< or =2.21	< or =3.50
75 years	< or =2.16	< or =3.43
76 years	< or =2.10	< or =3.35
77 years	< or =2.05	< or =3.26

78 years	< or =2.00	< or =3.17
79 years	< or =1.94	< or =3.08
80 years	< or =1.89	< or =2.99
81 years	< or =1.84	< or =2.91
82 years	< or =1.80	< or =2.84
83 years	< or =1.75	< or =2.78
84 years	< or =1.71	< or =2.73
85 years	< or =1.68	< or =2.69
86 years	< or =1.65	< or =2.67
87 years	< or =1.64	< or =2.65
88 years	< or =1.63	< or =2.64
> or =89 years	< or =1.62	< or =2.64

Interpretation

The values for the D-2-hydroxyglutaric acid and L-2-hydroxyglutaric acid concentrations are reported. The interpretation of the result must be correlated with clinical and other laboratory findings.

Cautions

No significant cautionary statements

Clinical Reference

1. Kranendijk M, Struys EA, Salomons GS, Van der Knaap MS, Jakobs C. Progress in understanding 2-hydroxyglutaric acidurias. J Inherit Metab Dis. 2012;35(4):571-587. doi:10.1007/s10545-012-9462-5

2. Muhlhausen C, Salomons GS, Lukacs Z, et al. Combined D2-/L2-hydroxyglutaric aciduria (SLC25A1 deficiency): clinical course and effects of citrate treatment. J Inherit Metab Dis. 2014;37(5):775-781. doi:10.1007/s10545-014-9702-y

3. Struys EA. D-2-Hydroxyglutaric aciduria: unravelling the biochemical pathway and the genetic defect. J Inherit Metab Dis. 2006;29(1):21-29. doi:10.1007/s10545-006-0317-9

4. Perales-Clemente E, Hewitt AL, Studinski AL, et al. Bilateral subdural hematomas and retinal hemorrhages mimicking nonaccidental trauma in a patient with D-2-hydroxyglutaric aciduria. JIMD Rep. 2020;58(1):21-28. doi:10.1002/jmd2.12188

Performance

Method Description

Urine volumes are spiked with a mixture of internal standards and evaporated. The dry residue is derivatized to form the diastereomeric molecules, then acidified and extracted. After evaporation, the dry residue is derivatized esters at the carboxylic acid moiety. Specimens are then analyzed by capillary gas chromatography mass spectrometry selected ion monitoring using chemical ionization, with chromatographic separation of the L,L- and D,L-diastereoisomers of derivatized 2-hydroxyglutaric acid (2-HGA), corresponding to L-2-HGA and D-2-HGA, respectively.(Unpublished Mayo method)

PDF Report

No

Day(s) Performed
Thursday

Report Available
3 to 9 days

Specimen Retention Time
2 months

Performing Laboratory Location
Mayo Clinic Laboratories - Rochester Main Campus

Fees & Codes

Fees
- Authorized users can sign in to Test Prices for detailed fee information.
- Clients without access to Test Prices can contact Customer Service 24 hours a day, seven days a week.
- Prospective clients should contact their account representative. For assistance, contact Customer Service.

Test Classification
This test was developed and its performance characteristics determined by Mayo Clinic in a manner consistent with CLIA requirements. It has not been cleared or approved by the US Food and Drug Administration.

CPT Code Information
83921 x 2

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
2HGA	D-,L- 2-Hydroxyglutaric Acid, QN, U	79297-8

Result ID	Test Result Name	Result LOINC® Value
614619	Interpretation	79303-4
614620	D-2-Hydroxyglutaric acid	80100-1
614621	L-2-Hydroxyglutaric acid	80099-5
614622	Reviewed By	18771-6