علامت های اختصاری اختلالات متابولیک ارثی

Amino Acid Disorders	
Disease	**Abbreviation**
Argininemia (arginase deficiency)	ARG
Argininosuccinic acidemia (argininosuccinate lyase deficiency)	ASA
Benign hyperphenylalaninemia (phenylalanine hydroxylase deficiency)	H-PHE
Defect of biopterin cofactor biosynthesis (pyruvoyltetrahydropterin synthase deficiency)	BIOPT (BS)
Defects of biopterin cofactor regeneration (dihydropteridine reductase deficiency)	BIOPT (Reg)
Carbamoyl phosphate dehydrogenase deficiency	CPS
Classic phenylketonuria (phenylalanine hydroxylase deficiency)	PKU
Citrullinemia type I (argininosuccinate synthase deficiency)	CIT-I
Citrullinemia type II (citrin deficiency)	CIT-II
Homocystinuria (cystathionine β-synthase deficiency)	HCY
Hypermethioninemias (methionine adenosyltransferase I/III deficiency, S-adenosylhomocysteine hydrolase deficiency, glycine N-methyltransferase deficiency)	MET
Maple syrup urine disease (branched-chain ketoacid dehydrogenase complex deficiency)	MSUD
Orotic aciduria (ornithine transcarbamylase deficiency)	OTC
Tyrosinemia type I (fumarylacetoacetate hydrolase deficiency)	TYR-I
Tyrosinemia type II (tyrosine transaminase deficiency)	TYR-II
Tyrosinemia type III (4-hydroxyphenylpyruvate hydroxylase deficiency)	TYR-III
Organic Acid Disorders	
β-Ketothiolase deficiency (mitochondrial acetoacetyl-CoA thiolase deficiency)	BKT
Ethylmalonic encephalopathy	EE
Glutaric acidemia type I (glutaryl-CoA dehydrogenase deficiency)	GA-I
Glutaric acidemia type II (multiple acyl-CoA dehydrogenase deficiency)	GA-II
3-Hydroxy-3-methyglutaric aciduria (3-hydroxy-3- methylglutaryl-CoA lyase deficiency)	HMG
Isobutyrylglycinuria (isobutyryl-CoA dehydrogenase deficiency)	IBG
Isovaleric acidemia (isovaleryl-CoA dehydrogenase deficiency)	IVA
Malonic acidemia (malonyl-CoA decarboxylase deficiency)	MAL
2-Methyl-3-hydroxybutyric aciduria (2-methyl-3-hydroxybutyryl-CoA dehydrogenase deficiency)	2M3HBA
Isolated 3-methylcrotonyl-CoA carboxylase deficiency	3MCC
3-Methylglutaconic aciduria (3-methylglutaconyl-CoA hydratase deficiency)	3MGA
Methylmalonic acidemia (Methylmalonyl CoA mutase deficiency)	MUT
Methylmalonic acidemia (Adenosylcobalamine synthesis defects)	Cbl A, Cbl B
Methylmalonic acidemia & homocystinuria (Methylmalonyl CoA mutase, Homocysteine: methylene tetrahydrofolate reductase methyltransferase deficiency)	Cbl C, Cbl D
Multiple carboxylase deficiency (Holocarboxylase synthetase deficiency)	MCD
Propionic acidemia (propionyl-CoA carboxylase deficiency)	PA
2-short/branched chain acyl-CoA dehydrogenase deficiency	2MBG
Fatty Acid Oxidation Disorders	
Carnitine-acylcarnitine translocase deficiency	CACT
Carnitine palmitoyltransferase I deficiency	CPT-I
Carnitine palmitoyltransferase II deficiency	CPT-II
Carnitine uptake defect	CUD
2,4-Dienoyl-CoA reductase deficiency	DE-RED
Long-chain L-3-hydroxyacyl-CoA dehydrogenase deficiency	LCHAD
Medium-chain acyl-CoA dehydrogenase deficiency	MCAD
Short-chain acyl-CoA dehydrogenase deficiency	SCAD
Trifunctional protein deficiency	TFP
Very long-chain acyl-CoA dehydrogenase deficiency	VLCAD

Nomenclature and abbreviations used are those accepted by the ACMG.

اختلالات متابولیسم اسیدهای آمینه

Entry	IMD	Primary Marker	Secondary Marker	Confirmatory Tests
1	**PKU** **H-PHE** **261600**	↑Phe [8, 10-20] ↓Tyr [10-12, 18]	↑Phe/Tyr [8, 11-14,16-18]	**AA plasma profile**: ↑Phe, ↓Tyr [8, 13]. **OA urine profile**: ↑Phenylacetate, ↑phenyllactate, ↑phenylpyruvate, ↑4-hydroxyphenyllactate, ↑4-hydroxyphenylpyruvate, ↑2-hydroxyphenylacetate, ↑mandelate [18, 19, 21].
2	**BIOPT [Reg]** **261630**	↑Phe [8, 13, 14, 16]	↑Phe/Tyr [8, 13, 14, 16]	**AA plasma profile:** ↑Phe [13]. **Urine biopterins** [8, 13, 31]. **Enzymatic assay and molecular studies** [31].
3	**BIOPT [BS]** **261640**	↑Phe [8, 13, 14, 16]	↑Phe/Tyr [8, 13, 14, 16]	**AA plasma profile:** ↑Phe [13]. **Urine biopterins** [8, 13, 31]. **Enzymatic assay and molecular studies** [31].
4	**MSUD** **248600**	↑Xle [8, 10, 11, 13-17, 18-20] ↑Val [8, 10, 11, 13-18, 18-20]	↑ Xle/Phe [8, 14, 17, 22] ↑Xle/Ala [8, 11, 14] ↑Val/Phe [8, 14]	**AA plasma profile**: ↑Leu, ↑Ile, ↑Val, ↑AlloIle [13, 23, 24]. **OA urine profile**: ↑2-Ketoisocaproate, ↑2-ketoisovalerate, ↑2-keto-3-methylvalerate, ↑2-hydroxyisocaproate, ↑2-hydroxyisovalerate, ↑2-hydroxy-3-methylvalerate, ↑phenyllactate, ↑phenylpyruvate [13, 18-20].
5	**ASA** **207900**	↑Cit [8, 10, 11, 13-18, 20, 25] ↑Asa [8, 18]	↑Asa/Arg [8] ↑ Cit/Arg [8, 14, 17] ↑ Orn [10, 11]	**AA plasma profile**: ↑Asa [13, 25]. **Molecular studies** [20].
6	**CIT I** **215700**	↑Cit [8, 10, 11, 13-16, 18, 20]	↑Cit/Arg [8, 14]	**AA plasma profile**: ↑Cit [13].
7	**CIT II** **605814**	↑Cit [8, 14, 15, 18-20] ↑Arg [8, 19] ↑Met [8, 19] ↑Thr [8]	↑Cit/Arg [14]	**Molecular studies** [26].
8	**HCY** **236200**	↑Met [8, 10, 11, 13-16, 18, 20]	↑Met/Phe [8, 11, 14]	**AA plasma profile**: ↑Hcy, ↑Met [13, 16]. **OA urine profile**: ↑Methylmalonate in Cbl C, D, F synthesis defects [13].
9	**MET** **250850**	↑Met [8, 10, 14, 16-18]	↑Met/Phe [8, 14, 17]	**AA plasma profile:** ↑Met [27].
10	**TYR I** **276700**	↑Suac [8, 11, 12, 14, 18, 19]	↑Tyr [11, 13, 14, 16, 18-20] ↑Tyr/Cit [14]	**AA plasma profile:** ↑Tyr, ↑Met [13]. **OA urine profile:** ↑Succinylacetone, ↑4-hydroxyphenylacetate, ↑4-hydroxyphenyllactate, ↑4-hydroxyphenylpyruvate [13, 18, 19].
11	**TYR II** **276600**	↑Tyr [8, 10, 13-16, 18]	↑Tyr/Cit [14]	**AA plasma profile:** ↑Tyr [13]. **OA urine profile:** ↑*N*-acetyltyrosine, ↑4-hydroxyphenylacetate, ↑4-hydroxyphenyllactate, ↑4-hydroxyphenylpyruvate [18, 21].
12	**TYR III** **276710**	↑Tyr [8, 14, 16, 18, 28]	↑Tyr/Cit [14]	**Molecular studies** [28, 29].
13	**ARG** **207800**	↑Arg [8, 11, 13-15, 17-19, 30]	↑Cit/Arg [8] ↑Arg/Orn [17]	**AA plasma profile:** ↑Arg [13, 30].
14	**OTC** **311250**	↓Cit [18, 19, 32]		**↑Urinary orotate** [19, 32]. **Enzymatic assay** [33].
15	**CPS** **237300**	↓Cit [18, 19, 32]		**Enzymatic assay and molecular studies** [34].
16	**NKH** **605899**	↑Gly [14, 18, 19]	↑Gly/Ala [14]	**↑CSF Gly /plasma Gly** [35].
17	**HHH** **238970**	↑Orn [18]		**Plasma AA:** ↑Orn, ↑Gln [36]. **OA urine profile:** Homocitrulline, orotate [36].

Nomenclature and abbreviations used are those accepted by the ACMG (See tables 1-2). The number down the disorder abbreviation represents the Online Mendelian Inheritance in Man (OMIM®) number. CSF: Cerebrospinal fluid.

اختلالات ارگانیک اسیدها

Entry	IMD	Primary Marker	Secondary Marker	Confirmatory Tests
1	**PA** **606054**	↑C3 [8-14, 16-19, 37]	↑C3/C2 [8, 10-12, 14, 16, 37] ↑C3/C16 [8, 10, 12, 14, 18] ↑C3/C0 [18] ↑Gly [18, 19] ↑C3/C4 [18]	**OA urine profile**: ↑3-Hydroxypropionate, ↑methylcitrate, ↑tiglylglycine, ↑propionylglycine [13, 17, 19, 37, 38].
2	**MUT** **609058** **Cbl A** **251100** **Cbl B** **251110** **Cbl C** **277400** **Cbl D** **277410**	↑C3 [8-14, 16-19, 37]	↑C3/C2 [8, 10-12, 14, 16, 37] ↑C3/C16 [8, 10, 12, 14, 18, 37] ↑C3/Met [14] ↑C4DC [9, 17, 18] ↑C3/C0 [18] ↑Gly [18] ↑C3/C4 [18]	**OA urine profile:** ↑Methylmalonate, ↑methylcitrate, ↑3-hydroxypropionate, ↑propionylglycine [13, 19, 21, 37, 38].
3	**MCD** **253270**	↑C5OH [8, 9, 13, 14, 16-18, 37]	↑C3 [8, 9, 13, 16-18] ↑C3/C2 [37] ↑C5-OH/C8 [14] ↑C5:1 [37]	**OA urine profile:** ↑3-Hydroxyisovaleric acid, ↑lactic acid, ↑methylcitric acid, ↑3-hydroxypropionic acid, ↑3-methylcrotonylglycine, ↑tiglylglycine, ↑pyruvate, ↑acetoacetate, ↑3-hydroxybutyrate [13, 18, 21, 39, 40].
4	**IBG** **611283**	↑C4 [8, 9, 14, 16, 18, 41-44]	↑C4/C2 [8, 14, 41] ↑C4/C3 [8, 14, 43] ↑C4/C8 [8, 14]	**OA urine profile:** ↑Isobutyrylglycine with no elevation of ethylmalonate [42-44]. **Urine acylcarnitines:** ↑C4 [43].
5	**EE** **602473**	↑C4 [9, 14, 19, 45, 46]	↑C5 [9, 14, 46]	**AC plasma:** ↓C2, ↑C4, ↑C5 [46]. **OA urine profile:** ↑Ethylmalonate, ↑methylsuccinate, ↑lactate, ↑2-ethyl-3-hydroxypropionate, ↑2-methylbutyrylglycine, ↑isovalerylglycine, ↑butyrylglycine, ↑isobutyrylglycine [19, 45-47].
6	**GA-1** **231670**	↑C5DC [8, 10, 11, 13, 14, 16-19, 37, 48, 50, 51, 53]	↑C5DC/C5OH [8, 14] ↑C5DC/C8 [8, 14, 18] ↑C5DC/C16 [8, 10, 14, 48] ↑C5DC/C4 [18] ↑C5DC/C12 [11, 18] ↑C5DC/C0 [48] ↑C5DC/[C8+C10] [48] ↑C5DC/C10OH [9]	**AC plasma profile:** ↑C5DC [13, 49]. **OA urine profile:** ↑Glutarate, ↑3-hydroxyglutarate, ↑glutaconate, ↑glutarylglycine [13, 19, 21, 37, 48-53]. **Molecular studies or enzymatic assay** [49].
7	**IVA** **243500**	↑C5[8-11, 13, 14, 16-19, 54, 56]	↑C5/C0 [8, 14] ↑C5/C2 [8, 14, 56] ↑C5/C3 [8, 14, 18, 56] ↑C5/C4 [18] ↑C5/C8 [18]	**OA urine profile:** ↑3-Hydroxyisovalerate, ↑isovalerylglycine. [13, 18, 19, 21, 38, 54-56].
8	**2MBG** **610006**	↑C5[8-10, 13, 14, 16, 56-58]	↑C5/C0 [8, 14] ↑C5/C2 [8,14, 56] ↑C5/C3 [8, 14, 56]	**OA urine profile:** ↑2-Methylbutyrylglycine [21, 56, 57, 59]. ↑2-ethylhydracrylate. [13, 57, 58].
9	**BKT** **203750**	↑C5:1 [8, 9, 11, 13, 14, 16-18, 37, 58, 60]	↑C5-OH [8-11, 13, 14, 16-18, 37, 58, 60] ↑C5-OH /C8 [8, 14] ↑C4OH [8, 60]	**OA urine profile:** ↑2-Methyl 3-hydroxybutyrate, ↑2-methylacetoacetate, ↑tiglylglycine, ↑2-keto-3-methylvalerate, ↑methylglutaconate, ↑3-hydroxybutyrate [13, 21, 37, 58, 60, 61].
10	**2M3HBA** **300438**	↑C5OH [8, 9, 14, 18, 58, 62] ↑C5:1 [8, 41, 58, 63] ↑C5OH/C8 [8, 14]		**OA urine profile:** ↑2-Methyl-3-hydroxybutyrate, ↑tiglylglycine [21, 41, 58, 62, 63].
11	**HMG** **246450**	↑C5-OH [8, 9, 13, 14, 16-18, 37, 66]	↑C6DC [8, 9, 14, 16, 66] ↑C5-OH/C0[8] ↑C5-OH/C8[8, 14]	**OA urine profile:** ↑3-Hydroxy-3-methylglutarate, ↑3-methylglutaconate, ↑3-methylglutarate, ↑3-hydroxyisovalerate, ↑3-methylcrotonylglycine [13, 17, 21, 64-66].
12	**3MGA** **250950**	↑C5-OH [8, 9, 13, 14, 18].	↑C5-OH/C8 [8, 14].	**OA urine profile:** ↑3-Methylglutaconate, ↑3-methylglutarate, ↑3-hydroxyisovalerate [13, 21, 67].
13	**3MCC** **210200**	↑ C5-OH[8, 9-11, 13, 14, 16-19, 37] ↑C5:1[18]	↑C5-OH/C8 [8, 14] ↑C5-OH/C0 [8, 14] ↑C5:1 [16, 37]	**AC urine profile:** ↑C5:1 [41]. **OA urine profile:** ↑3-Hydroxyisovalerate, ↑3-methylcrotonylglycine, ↑2-methyl-3-hydroxybutyrate, ↑tiglylglycine [8, 13, 19, 21, 41].
14	**MAL** **248360**	↑C3DC [8, 9, 14, 18] ↑C3DC/C10 [8, 14]		**OA urine profile:** ↑Malonate [68-70].
15	**PCD** **266150**	↑Cit [14]	↑Cit/Arg [14]	**Enzymatic assay** [71].

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اختلالات متابولیسم اسیدهای چرب

Entry	IMD	Primary Marker	Secondary Marker	Confirmatory Tests
1	**CUD OMIM 212140**	↓C0 [8, 14-16, 18, 72, 73] ↓C2 [72] ↓C3 [9] ↓C16 [9] ↓C18 [9]	↓ACs*/Cit [8, 14]	**Carnitine uptake in fibroblasts** [74]. **Enzymatic assay**: ↓Carnitine transporter [OCTN2] activity in fibroblasts [73, 75, 76]. **Molecular studies** [73].
2	**SCAD 201470**	↑C4 [8-10, 13-18, 37, 42, 72]	↑C4/C2 [8,14] ↑C4/C3 [8,14] ↑C4/C8 [8,14]	**OA urine Profile**: ↑Ethylmalonate, ↑butyrylglycine, ↑methylsuccinate, ↑adipate, ↑suberate, ↑sebacate [13, 21, 42, 44]. **Fibroblasts enzymatic assay** [42]. **Molecular studies** [42, 44].
3	**MCKAT 602199**	↑C6 [9] ↑C8 [8, 9, 14, 18, 72] ↑C8OH [72] ↑C3DC [8, 9] ↑C10OH [18, 72]	↑C8/C2 [14] ↑C8/C10 [14] ↑C5DC/C10OH [9]	**Enzymatic assay** [77].
4	**MCAD 201450**	↑C8 [8- 11, 13- 19, 37, 72]	↑C6 [8- 12, 14-19, 37, 72] ↑C10 [8-15, 18, 37, 72] ↑C10:1 [8-12, 14-19, 37, 72] ↑C8/C2 [8, 12, 14] ↑C8/C6 [18] ↑C8/C10 [8, 12, 14, 16, 18]	**OA urine Profile**: ↑Hexanoylglycine, ↑suberylglycine, ↑5-hydroxyhexanoate, ↑7-hydroxyoctanoate, ↑adipate,↑suberate, ↑sebacate, ↑octanedioate, ↑decanedioate, ↑phenylpropionylglycine [13, 19, 21].
5	**GA-II 231680**	↑C8 [8-10, 16-19, 37] ↑C10 [9, 10, 17, 19, 37]	↑C4 [8-10, 16, 18, 19, 37, 72] ↑C5 [8-10, 16, 18, 72] ↑C5DC [8, 16, 18, 72] ↑C6 [9, 16, 18, 19, 37, 72] ↑C12 [9, 10, 16, 18, 19, 72] ↑C14:1 [9, 19, 37] ↑C14 [8-10, 16, 18, 19] ↑C16 [10, 19, 72] ↑C18:1 [9, 19] ↑C18 [9, 20]	**OA urine Profile:** ↑Glutarate ↑ ethylmalonate, ↑hexanoylglycine, ↑adipate, ↑suberate, ↑sebacate, ↑2-hydroxyglutarate, ↑isovalerylglycine, ↑isobutyrylglycine, ↑2-methylbutyrylglycine, ↑phenylpropionylglycine, ↑suberylglycine [13, 19, 21].
6	**DE-RED 222745**	↑C10:2 [8, 9, 14, 18, 72] ↑C10:2/C10 [14]		**Enzymatic assay** [78].
7	**VLCAD 201475**	↑C14:1 [8-11, 13-16, 18, 37, 72]	↓C0 [13] ↑C14 [8-11, 13-16, 18, 37, 72] ↑C14:2 [8, 13, 14, 72] ↑C16 [9, 10, 16, 18, 72] ↑C18:1 [9, 11, 16, 18, 72] ↑C18 [9, 11, 72] ↑C14:1/C12:1 [16] ↑C14:1/C2 [8] ↑C14:1/C4 [18] ↑C14:1/C5 [18] ↑C14:1/C8 [18] ↑C14:1/C16 [8, 14] ↑C12 [9] ↑C18:2 [9]	**OA urine Profile**: ↑Suberate, ↑sebacate, unsaturated species [21]. **Enzymatic assay and molecular studies** [79, 80].
8	**CPT-IA 600528 CPT-IB 601987**	↓C16 [8-10, 13, 14, 18, 19, 57, 72, 81]	↑C0 [8-10, 13, 14, 18, 19, 57, 81] ↓C18:1 [9, 10, 72] ↓C18 [8-10, 13, 14, 18, 19, 57, 72, 80] ↑C0/C16+C18 [8, 14, 15, 18, 19, 57, 81]	**Enzymatic assay and molecular studies** [57, 81, 82].
9	**CACT 212138**	↑C16 [8, 9, 13, 14, 16, 18, 72, 83]	↑C14 [8, 9] ↑C14:1 [9] ↑C18:1 [9, 14, 16, 72, 83] ↑C18:2 [9, 14] ↑C18 [8, 9, 13, 14, 83] ↓C0/C16+C18 [14] ↓C0 [13, 83]	**Enzymatic assay** [84, 85].
10	**CPT II 255110**	↑C16 [8-10, 13-19, 37, 72]	↓C0 [10, 13] ↑C14 [8, 9] ↑C16:1 [19] ↑C18 [8-10, 13-15, 19, 72] ↑C18:1 [9, 10, 14, 16, 18, 19, 72] ↑C18:2 [9, 14] ↑C16+C18:1/C2 [8, 18] ↓C0/C16+C18 [14]	**Enzymatic assay and molecular studies** [82, 85].
11	**LCHAD 609016**	↑C16-OH [8, 9, 11, 14, 16-18, 72] ↑C18OH [7, 8, 9, 11, 14, 86] ↑C18:1OH [7, 8, 9, 11, 14, 16, 72, 86-88] ↑C16OH/C16 [7, 8, 14, 86] ↑C18OH/C18 [7, 86]	↑C16:1OH [7, 8, 9, 14, 86] ↑C14:1 [7, 9, 11, 86, 87] ↑C14 [7, 9, 11, 87] ↑C14OH [9, 11, 87] ↑C14:2 [7, 87] ↑C16 [9, 11, 87] ↑C18:1 [9, 87] ↑C18:2 [9, 87]	**OA Profile**: ↑Adipate, ↑suberate, ↑sebacate, ↑2-hydroxyadipate, ↑3-hydroxyadipate, ↑3-hydroxyoctenedioate, ↑3-hydroxysuberate, ↑3-hydroxydecanedioate, ↑3-hydroxy-sebacate, ↑ 3-hydroxydodecenedioate, ↑3-hydroxydodecanedioate, ↑3-hydroxytetradecenedioate, ↑3-hydroxytetradecanedioate. [13, 21]. **Plasma AC**: ↑C12, ↑C14, ↑C16, ↑C14:1, ↑C14:2, ↑C18:1, ↑C18:2, ↑C16OH, ↑C18:1OH, ↑C14:1OH, ↑C14:OH [87]. **Enzymatic assay and molecular studies** [11, 87, 88].
12	**TFP 609015**	↑C16-OH [8, 9, 11, 14, 16-18, 72] ↑C18OH [7, 8, 9, 11, 14, 86] ↑C18:1OH [7, 8, 9, 11, 14, 16, 72, 86-88] ↑C16OH/C16 [7, 8, 14, 86] ↑C18OH/C18 [7, 86]	↑C16:1OH [7, 8, 9, 14, 86] ↑C14:1 [7, 9, 11, 86, 87] ↑C14 [7, 9, 11, 87] ↑C14OH [9, 11, 87] ↑C14:2 [7, 87] ↑C16 [9, 11, 87] ↑C18:1 [9, 87] ↑C18:2 [9, 87]	**OA Profile**: ↑Adipate, ↑suberate, ↑sebacate, ↑2-hydroxyadipate, ↑3-hydroxyadipate, ↑3-hydroxyoctenedioate, ↑3-hydroxysuberate, ↑3-hydroxydecanedioate, ↑3-hydroxy-sebacate, ↑ 3-hydroxydodecenedioate, ↑3-hydroxydodecanedioate, ↑3-hydroxytetradecenedioate, ↑3-hydroxytetradecanedioate. [13, 21]. **Plasma AC**: ↑C12, ↑C14, ↑C16, ↑C14:1, ↑C14:2, ↑C18:1, ↑C18:2, ↑C16OH, ↑C18:1OH, ↑C14:1OH, ↑C14:OH [87]. **Enzymatic assay and molecular studies** [11, 87, 88].

Nomenclature and abbreviations used are those accepted by the ACMG (See tables 1-2). The number down the disorder abbreviation represents the OMIM® number. *ACs: Sum of selected acylcarnitines (C0+C2+C3+C16+C18+C18:1).