**Supplementary Table 1.** Clinical characteristics of patients with type I and II sialidosis.

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| **Authors** | **Number of patients (n)** | **Ethnicity** | **Genetic Alterations** | **Type of alteration** | **Age at onset** | **Age at evaluation** | **Ophthalmologic findings** | **Neurologic findings** | **Skeletal findings** | **Other**  **findings** | **EEG and Brain Imaging** | **EKG** | **Cardiovascular findings including ECHO** |
| Bonten et al.1 | 11  (5 type I,  6 type II) | 2 African American  2 Italian  1 Greek  2 German  1 Dutch  1 Hispanic  2 Unknown(Caucasian) | Patient 1: Arg294Ser,Leu231His (Compound Heterozygous)  Patient 2: Arg296Ser, Gly218Ala (Compound Heterozygous)  Patient 3:Gly227Arg (Homozygous)  Patient 4: Gly227Arga (Homozygous)  Patient 5 and 6 (siblings): Val54Met, Gly378stop (Compound Heterozygous)  Patient 7: Gly328Ser, Dupl399HisTyr (Compound Heterozygous)  Patient 8: Tyr370Cys (Homozygous)  Patient 9: Phe260Tyr (Homozygous)  Patient 10:Phe260Tyr,Leu363pro (Compound Heterozygous)  Patient 11:Arg280stop,Pro335Gln (Compound Heterozygous) | Point mutations, deletions and insertion | Mean:7.86 yrs  (20 wk gestational period-17 yrs) | Mean:7.61yrs  (4 months-44 yrs (death) | Cherry-red spots: 5/11  (macular 1)  Visual acuity:  diminution: 2/11  Ocular lens opacities: 2/11  Prolonged latencies on visual evoked potentials:1/11  Intolerance to light: 1/11 | Seizures: 5/11(myoclonus 4)  Ataxia: 4/11  Slurred speech:1/11  Dysmetria: 2/11  Microcephaly: 1/11  Hearing loss: 4/11  (Sensorineural deafness 1)  Moderate delay in speech: 1/11  Spasticity: 1/11  Hypotonia: 3/11  Cerebellar signs: 1/11  Dysarthria: 3/11  Dysphagia: 1/11  Dydiadchokinesia: 1/11  Pyramidal signs: 1/11  Axonal polyneuropathy: 1/11  Orbital hypoplasia: 1/11  Mental retardation:mild(1/11)  Developmental delay: 4/11  Hydrocephalus: 1/11 | N/A | N/A | EEG:Abnormal 2/11 (1with normal and 1 with borderline IQ) | Non-specific alterations of repolarization (1/11) | Normal ECHO 4/11  Cardiomegaly/Cardiomyopathy 2/11 (both type II) |
| Itoh et al2 | 4  [2 type I(mild juvenile-onset)  2 type II(congenital form)] | Japanese (East Asian) | Type II: C239T (P80L), T718C (W240R) (Compound Heterozygous)  Type I: C946T (p.P316S) (Homozygous) | Missense  mutation | Fetal life (21 to 33 weeks’ gestation), Type I 14 yrs | Birth, 24 yrs (Type I) | Bilateral cherry-red spots | Ataxia, dysgraphia, generalized tonic clonic seizures, dysarthria, action myoclonus | N/A | Hepatosplenomegaly, ascites | N/A | N/A | N/A |
| Lukong KE et a34 | 9  (2 type I,  7 type II) | Patient 1: Mexican  Patient 2: American (Caucasian)  Patient 3: Ashkenazi Jewish  Patient 4: Chinese (East Asian)  Patient 5: Turkish  Patient 6: Polish  Patient 7 and 8 (siblings): Spanish  Patient 9: Italian | Patient 1 and 2: Gly227Arg (Homozygous)  Patient 3: Ala298Val (Homozygous)  Patient 4: Ser182Gly (Homozygous)  Patient 5: Frameshift, Stop904 \*deletion (Homozygous)  Patient 6: Gly68Val (Homozygous)  Patient 7 and 8: Leu270Phe (Homozygous)  Patient 9: Gly328Ser (Compound Heterozygous) | Missense mutations and a deletion | 10.84yrs  (3 months-24 yrs) | N/A | Cherry-red spots: 4/9 | Seizures: 2/9  Ataxia: 1/9  Mental retardation: 3/9  Myoclonus: 2/9 | Skeletal dysplasia 1/11 | Hydrops fetalis: 4/11  Nephrosialidosis: 1/11  Mild dysphagia: 1/9 | N/A | N/A | N/A |
| Naganawa et al4 | 2 (type I) | Japanese (East Asian) | G649A (V217M), G727A (G243R) (both Compound Heterozygous) | N/A | 17 & 32 yrs | 25 & 42 yrs | Lens opacities, macular cherry-red spots | Ataxic gait, speech disturbance, generalized tonic clonic seizures, dysarthria, action myoclonus, hyperactive deep tendon reflexes | N/A | N/A | Normal MRI brain | N/A | N/A |
| Oohira Tet al5 | 1 (type II) | Japanese (East Asian) | N/A | N/A | 14 days | 5 years | Macular cherry-red spots | Mental retardation, myoclonus, cerebellar ataxia, brisk tendon reflexes, positive Babinski sign, | Coarse facies, dislocation of hip joints, contractures of the first fingers of both hands, scoliosis, oar like ribs, vertebral hypoplasia | Congenital adrenal hyperplasia, hepatosplenomegaly, gingival hyperplasia, short stature | CT scan: Mild brain atrophy | N/A | Grade 2/6 systolic murmur |
| Pattison S et al6 | 4 (type II) | 1 Czech (Ashkenazi Jewish)  1 Irish/French Canadian  2 Mennonites | G674C (p.R225P), C893T (p.A298V), G3A (p.M1?), C941G (p.R341G), and G69A (p.W23X) | Missense (4) and 1 nonsense. | N/A | N/A | N/A | N/A | N/A | N/A | N/A | N/A | N/A |
| Penzel R et al7 | 1 (female, type II) | Not known | G2736C transversion (Homozygous) | Transversion (Intronic) | 27 weeks’ gestation | 27 weeks’ gestation | N/A | Myoclonus | N/A | Ascites, edema, hydrops fetalis | Fine calcifications of the thalamic striatal blood vessels on cranial USG | N/A | N/A |
| Sergi C et al8 | 2 (type II) | Turkish | W29X (substitution of tryptophan at codon 29 by a termination codon) | Nonsense mutation | Patient 1: Delivered at 26 weeks’ gestation and died at 2 months  Patient 2: Pregnancy terminated at 20 weeks’ gestation | N/A | N/A | N/A | N/A | Hydrops fetalis, hepatomegaly, respiratory distress syndrome, and anemia | N/A | N/A | N/A |
| Seyrantepe V et al9  Ledvinova J et al10 | 4 (type I) | 2 Czech  2 French | 2 Czech patients C1034T (T345I) (Homozygous)  French Patient 1 G407E p.G136E and T824C p.V275A (Compound Heterozygous)  French Patient 2 (Type 1): T332C p.L111P (Heterozygous). Second mutation not determined. | 3 substitutions, 1 missense | N/A | 15.5 yrs  (14-20 yrs) | Ocular myoclonus, cherry-red spots | Myoclonus, tremor, partial complex seizures, progressive ataxia, dyskinetic extrapyramidal and cerebellar syndromes, quadriparesis, tremor, hyperreflexia | Dysostosis multiplex | N/A | N/A | N/A | N/A |
| Uhl J et al11 | 2 (type II) | Turkish | 11 kb deletion encompassing entire coding region of *NEU1* (Homozygous) | Deletion | Prenatally diagnosed | N/A | N/A | N/A | Polydactyly | Ascites, hydrops fetalis, hepatomegaly | N/A | N/A | N/A |
| Bonten E et al12 | 3  [2 type I(siblings), 1 type II] | Unknown | Patient 1 and 2 (siblings): G1258T transversion (Heterozygous) Patient 3: T 401G transversion (p.Leu91Arg) and a single-base  deletion at nucleotide 1337 (Compound Heterozygous) | Point mutations and a deletion | N/A | N/A | N/A | N/A | N/A | N/A | N/A | N/A | N/A |
| Lowden JA et al13 | 37 (18 type I, 19 type II) | 7 Italian  10 Japanese  5 Caucasian | N/A | N/A | Type 12.4 ± 4.7 yrs  Type 2  Juvenile 10.4 ± 5.3 yrs  Infantile: 0-10 months | N/A | Cherry-red spots (33/37), Corneal clouding/Lens opacities (17/37), loss of visual acuity (22/37) | Seizures (15/37), myoclonus (30/37), ataxia (15/37), pyramidal tract signs (7/37), mental retardation (10/37) | Coarse facies (19/37), Vertebral changes (18/37), Growth disturbance (16/37), | Visceromegaly (6/37), Foam cells (19/37), Hearing loss (9/37) | Abnormal EEG (13/37) | N/A | N/A |
| Sergi C et al14 | 1 (type II neonatal-onset) | Syrian | N/A | N/A | Prenatal diagnosis (27 weeks’ gestation) | N/A | Corneal clouding | N/A | Coarse facies | Visceromegaly, ascites, hydrops, inguinal hernia | Normal CNS ultrasound | N/A | Normal ECHO |
| Lemyre E et al15 | 3 (type II) | 3 French Canadian | N/A | N/A | 31-32 weeks’ gestation | Birth | Clear corneae, absence of cherry-red spot | Psychomotor retardation, hypotonia, nystagmus, decreased deep tendon reflexes | Coarse facies, widening of long bones and ribs, J-shaped sella turcica and calcaneal calcifications, dysostosis multiplex | Fetal ascite, nephrotic syndrome, heart failure, esophageal atresia type 3, gum hypertrophy, failure to thrive, hepatosplenomegaly, sensorineural deafness | N/A | N/A | Moderate LVH, cardiomegaly (patient 2 who died of heart failure) |
| Loren DJ et al16 | 1 (type II) | Caucasian | G45A (Exon 1) and G1022A (Exon 5) (Compound Heterozygous) | Nonsense and splice site mutations | Prenatal diagnosis (18 weeks’ gestation) | Birth | N/A | N/A | N/A | Polyhydramnios, ascites, lung involvement | N/A | N/A | N/A |
| Lee BH et al17 | 1 (type II) | Korean (East Asian) | C239T (p.Pro80Leu)  (Homozygous) | N/A | Prenatal diagnosis (22 weeks’ gestation) | Birth | Lack of visual fixation and ability to track objects | Hypotonia | Coarse facial features | Ascites, hydrops fetalis, cardiomegaly, hepatosplenomegaly, sparse facial hair, gum hypertrophy | N/A | N/A | Cardiomegaly, ventricular dilation, huge PDA which closed on day 15 |
| Tabardel Y et al18 | 1 (type II) | French | N/A | N/A | N/A | Birth | N/A | N/A | Facial dysmorphism | Hydrops fetalis, heart failure | N/A | N/A | N/A |
| Ahn JH et al19 | 1 (type I) | Korean (East Asian) | G928A (p.D310N), novel c.15\_16del (p.P6Qfs\*21)  (Compound Heterozygous) | N/A | 12 yrs | 36 yrs | Bilateral macular cherry-red spots, thickening of peripapillary retinal fiber layer in both eyes | Ataxia, myoclonus, generalized tonic clonic seizures, dysarthria | N/A | N/A | EEG 13 years spike and polyspike wave pattern, MRI mild cerebellar atrophy | N/A | N/A |
| Gultekin M et al20 | 1 (type I) | Turkish | NM\_000434:c.625delG (p.Glu209SerfsTer94) and novel NM\_000434:c.92G8A (p.Asp310Asn) (Compound Heterozygous) | Frameshift | 18 yrs | 24 yrs | Bilateral macular cherry-red spots | Truncal ataxia, dysarthria, intentional tremor of the upper limbs, generalized seizures | N/A | N/A | MRI: Mild brain atrophy | N/A | N/A |
| Ranganath P et al21 | 2 (1 type I , 1 type II) | South Asian | **Patient 1:** C880T transition in exon 5 (R294C) and a 1-base deletion at nucleotide 1191 (c.1191delG) in exon 6 (Compound Heterozygous)  **Patient 2:** Homozygous for a 1-base deletion at nucleotide 73 (c.73delG) | Missense and frameshift mutations | N/A | Patient 1: 14 yrs  Patient 2: 1.5 yrs | Bilateral fundal cherry-red spots, mild corneal haziness | Gait disturbance, dysarthria, myoclonic jerks, fine tremors at rest, dysmetria, nystagmus, gait ataxia, | Macrocephaly, coarse facies,  bilateral genu valgum | Protuberant tongue, gum hypertrophy, generalized hypertrichosis, large Mongolian spots on the back, umbilical hernia, hepatomegaly | N/A | N/A | Thickening of mitral valve leaflets with mitral valve prolapse/mitral regurgitation |
| Sekijima Y et al22 | 1 (type I) | Japanese | C239T (p.P80L), G403A (p.D135N) (Compound Heterozygous) | Missense | 14 years | 16 years | Bilateral macular cherry-red spots | Subnormal intelligence, dysarthria, myoclonus, intentional tremors, limb and gait ataxia, hyperreflexia | N/A | N/A | MRI Brain atrophy | N/A | Normal ECHO |
| Sobral I et al23 | 1 (type I) | Portuguese | G700A (p.D234N) exon 4, C1021T(p.R341X) exon 5 (Compound Heterozygote) | Truncated protein | 26 yrs | 53 yrs | Reduced visual acuity, bilateral cherry-red spots, atrophy of nerve fibers, visual field defects | Myoclonus, ataxic gait, dysarthria and difficulty in writing | N/A | N/A | N/A | N/A | N/A |
| Canafoglia L et al 24 | 6 (type 1) | Italian | c.200G>T, p.S67I (Homozygous), (G679A, p.G227R; C913T, p.R305C) (Compound Heterozygous) | N/A | 22-32 yrs | 27-42 yrs | Cataract | Late onset myoclonus, dysarthria | Femur head necrosis, scoliosis | N/A | Craniospinal MRI: Cerebellar vermis atrophy, syringomyelia; Somatosensory evoked potentials: Enlarged | N/A | N/A |
| Schene IF et al25 | 2 (type 1) | Dutch | c.1195\_1200dup p.His399\_Tyr400dup; G679A, p.Glu227Arg (Compound Heterozygous) | N/A | 12, 13 yrs | 14, 15 yrs | Nummular cataract, macular cherry-red spot, and optic nerve atrophy | Tremors, ataxia, myoclonus, downbeat nystagmus | Avascular osteonecrosis of right femoral head | N/A | Normal brain MRI | N/A | N/A |
| Mutze U et al26 | 1 (type 1) | German | C699CA, p.S233R in exon 4 and A803G; p.Y268C in Exon 5 (Compound Heterozygous) | Missense | N/A | 6 yrs | Macular cherry-red spots | Normal neurological examination | N/A | N/A | EEG: Generalized epileptic discharges; Visual evoked potentials: Prolonged bilaterally  Normal brain MRI | N/A | N/A |
| Gowda VK et al27 | 1 (type 1) | South Asian | G742G T (p.G248C) in exon 4 (Homozygous) | Missense | 9 yrs | 9 yrs | Bilateral macular cherry-red spots | Generalized tonic clonic seizures, ataxia, myoclonus, spasticity, increased deep tendon reflexes | N/A | N/A | Normal brain MRI and EEG | N/A | N/A |
| Aravindhan A et al28 | 1 (type 1) | Ecuadorian | C629T (p.Pro210Leu) (Homozygous) | Missense | 16 yrs | 39 yrs | Bilateral cherry-red spots | Generalized tonic clonic seizures, myoclonic seizures, broad based ataxic gait, truncal and appendicular ataxia | N/A | N/A | EEG: Revealed multiple brief myoclonic seizures and generalized slow spike/polyspike wave complexes | N/A | N/A |
| Hu SC et a29 | 1 (type 1) | East Asian | A544 G (Ser182Gly), C619T (termination codon) | Missens, nonsense | 12 yrs | 15 yrs | Bilateral cherry -red spots | Myoclonus, gradually progressive ataxia, tremors, and psychomotor and speech regression | N/A | N/A | EEG: Focal spikes arising from bilateral centrotemporal regions, followed by ictal myoclonic seizures with generalized muscle contraction activities lasting 15–20 s; MRI: Mild brain atrophy | N/A | N/A |
| Mohammed AN et al30 | 1 (type 1) | East Asian | A554G (p.S182G) and G679A (p.G227R) (Compound Heterozygous) | Missense | 12 yrs | 20 yrs | Normal | Ataxia, generalized tonic clonic seizures, myoclonus, saccadic hypometria, increased tone, brisk deep tendon reflexes | N/A | N/A | Normal EEG, Normal brain MRI | N/A | N/A |
| Cameron PD et al12 | 1 (type II) | Caucasian | N/A | N/A | Birth | Birth | Poor visual tracking | Absent auditory response, hypotonia | Facial dysmorphism, short stubby fingers and square set thumb | Hepatosplenomegaly, ascites | N/A | N/A | Cardiomegaly at birth, pulmonary edema |
| Copper A et al32 | 2 (type II) | Caucasian | N/A | N/A | Birth | 3 months | N/A | Delayed psychomotor development | Coarse facial features, | Hepatosplenomegaly | Normal CT brain | Left ventricular hypertrophy | Cardiomegaly on ECHO |
| Hale LP et al33 | 1 (type II) | African American | N/A | N/A | In utero | Birth | N/A | N/A | Short first metatarsals, epiphyseal stippling | Non-immune hydrops, ascites, gingival hypertrophy | N/A | N/A | Left ventricular dysfunction, right ventricular enlargement, vacuolation of myocytes on autopsy |
| Paschke et al34 | 1 (type II) | Austrian (Caucasian) | N/A | N/A | 10 weeks of age | 10 months | Normal fundus and corenae | Severe psychomotor retardation, seizures, hypertonia | Pectus excavatum | Hepatosplenomegaly | N/A | Right ventricular hypertrophy | Cardiomegaly, hypertrophic cardiomyopathy |
| Pueschel SM et al35 | 1 (type II) | Caucasian | N/A | N/A | In utero | Birth | N/A | Seizures | Coarse facies, anteverted nostrils, slight gibbus | Hepatosplenomegaly | N/A | N/A | Mild left ventricular dysfunction, diffuse LVH on ECHO; biventricular hypertrophy on autopsy; multiple clear vacuoles in myocardial cells |
| Schleutker J et al36 | 16 (type II) | Caucasian | N/A | N/A | Fetal life to late infancy | Birth to within the first few years of life | N/A | Delayed development, ataxia, seizures, hypotonia | Dysmorphism | Ascites, hepatosplenomegaly | N/A | N/A | Heart failure (2/16) |
| Kang E et al37 | 1 (type II) | East Asian | N/A | N/A | In utero (22 weeks’ gestation) | Birth | N/A | Hypotonia | Coarse facial features, dysostosis multiplex | Ascites, hepatomegaly, congenital diaphragmatic hernia | N/A | N/A | Persistent pulmonary hypertension |
| Huang YZ et al38 | 12 (type I) | East Asian | 10 S182G/S182G (Homozygous); 1 S182G/Q55X (Compound Heterozygous); 1 S182G/A319V (Compound Heterozygous) | N/A | 12-33 yrs | 26-50 yrs | Blurred vision (9/12) | Myoclonus, ataxia (gait, truncal), dysmetria, frequent falls |  |  | MRI: Cerebral atrophy (5/12), Cerebellar atrophy (1/12), Tiny bright dots in basal ganglia (2/12)  EEG: Paroxysmal diffuse theta waves (1/12)  NCV: Abnormal (6/12) | N/A | N/A |
| Young ID et al39 | 1 (type II) | South Asian | N/A | N/A | 18 months | 3 yrs | Cherry-red spots, extensive bilateral lens opacities | Delayed milestones, grand mal seizures, myoclonic seizures, ataxia, intention tremor, nystagmus, hypotonia, extensor plantar response | Coarse facial features, flattening of lumbar vertebrae, bony abnormalities | Gingival hypertrophy, | Delayed visually evoked potentials | N/A | N/A |
| Arora V et al40 | 7 (type 2) | South Asian | G679A (p.Gly227Arg) (Exon 4) (Homozygous) |  | 5 months to 6 yrs | 3-11 yrs | Cherry-red spot (6/7), Bull’s eye maculopathy (1/7) | Developmental delay (7/7), ataxia (2/7), seizures (2/7) | Coarse facial features (7/7), short stature (7/7), contractures (4/7), scoliosis (5/7), dysostosis (4/7) | Hearing loss, (4/7), hepatomegaly (4/7), Splenomegaly (2/7), hernia (1/7), Nephrosialidosis/single kidney (1/7) | MRI: Cerebral atrophy (1/7) | N/A | N/A |
| Lee YJ et al41 | 1 (type II) | Korean (East Asian) | C239T (p.Pro80Leu) (exon 2) (Homozygous) | Missense | In utero (19 weeks’ gestation) | 3 months | Bilateral congenital cataract with foveal hypoplasia | Hypotonia | Coarse facies | Fetal ascites, hepatosplenomegaly | N/A | N/A | N/A |
| Neeraja K et al42 | 2 (type 1) | South Asian | p.Arg294Cys (Homozygous), p.Arg305Pro (Homozygous) | Missense | N/A | N/A | No cherry-red spot | Ataxia, progressive myoclonus | N/A | N/A | N/A | N/A | N/A |
| Caciotti A et al43 | 2 (type II)  12 (type II) juvenile-onset from other studies  18 (type II) neonatal-onset from other studies | Italian | G679A (p.G227R) (Homozygous); splicing transition G807 + 1A (Homozygous) | Missense, splicing translation | Birth to 1 year | 1-9 yrs | Cherry-red spot (Infantile onset), cataract | Developmental delay, myoclonic jerks | Coarse facies, dysostosis multiplex | Hepatosplenomegaly, renal anomalies  Neonatal onset: ascites, edema, hydrops | N/A | N/A | Cardiac anomalies (1)  Juvenile-onset type II (3/12) cardiac abnormalities  Neonatal-onset type II (6/18) cardiac abnormalities |
| Godra A et al44 | 1 (type II) | N/A | N/A | N/A | In utero | Birth | N/A | N/A | N/A | Ascites, hepatomegaly | N/A | N/A | Enlarged ventricles, mild decrease in LV function, large PDA, cardiac dilation, vacuoles in myocytes |
| Chen CM et al45 | 2 (type 1) | East Asian | (A544G) (p.Ser182Gly) exon 3 (Homozygous) | Missense | 14-17 yrs | N/A | Optic atrophy | Ataxia, myoclonus, nystagmus | N/A | N/A | MRI: Mild cerebellar atrophy | N/A | N/A |
| Steinman L et al46 | 1 (type 1) | Mixed East Asian and Portuguese | N/A | N/A | 20 yrs | N/A | Cherry-red spot | Myoclonus, dysphagia, dysarthria | Clinodactyly of terminal phalanx of the fifth finger, mild clubbing of fingers | N/A | EEG: Abnormal; NCV: Abnormal; Visually evoked potentials: Abnormal | N/A | N/A |
| Varela MD et al47 | 7 (type 1) | N/A | N/A | N/A | 27.5+9.8 yrs |  | Lens opacities (8/8), optic atrophy (2/8), macular cherry-red spot (8/8), visual disability (2/8) | N/A | N/A | N/A | N/A | N/A | N/A |
| Palmeri S et al48 | 1 (type I) | Italian | N/A | N/A | 17 yrs | 17 yrs | Macular cherry-red spot | Ataxia, myoclonus, generalized epilepsy, nystagmus, dysarthria | N/A | N/A | MRI: Cerebellar atrophy EEG: Spikes preceding the myoclonus | N/A | N/A |
| Vieira de Rezende Pinto WB et al49 | 2 (1 type 1, 1 type 2) | Brazilian | N/A | N/A | 17, 23 yrs | 27, 30 | Bilateral macular cherry-red spots | Ataxia, slurred speech, dysarthria, dysmetria, hyperreflexia, myoclonic seizures | N/A | N/A | MRI: cerebral atrophy | N/A | N/A |
| Michalewska Z et al50 | 1 (type 1) | Polish | N/A | N/A | 15 yrs | 20 yrs | Bilateral macular cherry-red spot | Myoclonus, ataxia, generalized tonic-clonic and partial seizures, dystonia | N/A | N/A | MRI: Normal; EEG: discharges of sharp waves and diffuse theta waves | N/A | N/A |
| Heroman WJ et al51 | 1 (type 1) | Caucasian | N/A | N/A | 14 yrs | 14 yrs | Bilateral macular cherry-red spot | N/A | N/A | N/A | N/A | N/A | N/A |
| Rosenberg R et al52 | 2 (type II) | French | N/A | N/A | 3,5 yrs | N/A | Bilateral macular cherry-red spot | Hypotonia | Dysostosis | Hepatosplenomegaly, hearing loss, nystagmus | N/A | N/A | N/A |
| Ganguly S et al53 | 1 (type 1) | South Asian | N/A | N/A | 10 yrs | 12 yrs | Bilateral macular cherry-red spot | Myoclonus | N/A | N/A | N/A | N/A | N/A |
| Kersten HM et al54 | 1 (type 1) | Samoan | N/A | N/A | 22 yrs | 32 yrs | Bilateral macular cherry-red spot | Myoclonus, generalized tonic-clonic seizures | N/A | N/A | N/A | N/A | N/A |
| CoppolaA et al55 | 4 (type 1) | 3 Italian  1 Turkish | G982A (p.Gly328Ser, rs534846786), deletion c.1208delG (p.Ser403ThrfsTer85, rs1301852124) (Compound Heterozygous)  T272G (p.Leu91Arg, rs104893972) G982A (p.Gly328Ser, rs534846786) (Compound Heterozygote)  G914A (p.Arg305His, rs774362886) deletion of a nucleotide c.625delG, which determines a frameshift mutation p.Glu209SerfsTer94 (Compound Heterozygote)  c.1208delG (p.Ser403ThrfsTer85, rs1301852124) and G982A (p.Gly328Ser, rs534846786) (Compound Heterozygote) | Missense, frameshift and deletion | 12-17 yrs | 18-43 yrs | Bilateral cataract, cherry-red spots | Ataxia, nystagmus, dysarthria, dysmetria, myoclonus | N/A | N/A | MRI Brain: Cortical atrophy, cerebellar atrophy | N/A | N/A |

MRI=Magnetic resonance imaging; EEG=Electroencephalography; ECHO=Echocardiography; IQ=Intelligence quotient; LV=Left ventricle; LVH=Left ventricular hypertrophy; PDA=Patent ductus arteriosus; NCV=Nerve conduction velocity

**References**

1. Bonten EJ, Arts WF, Beck M, Covanis A, Donati MA, Parini R, Zammarchi E, d'Azzo A. Novel mutations in lysosomal neuraminidase identify functional domains and determine clinical severity in sialidosis. Hum Mol Genet. 2000 Nov 1;9(18):2715-25. doi: 10.1093/hmg/9.18.2715. PMID: 11063730.
2. Itoh K, Naganawa Y, Matsuzawa F, Aikawa S, Doi H, Sasagasako N, Yamada T, Kira J, Kobayashi T, Pshezhetsky AV, Sakuraba H. Novel missense mutations in the human lysosomal sialidase gene in sialidosis patients and prediction of structural alterations of mutant enzymes. J Hum Genet. 2002;47(1):29-37. doi: 10.1007/s10038-002-8652-7. PMID: 11829139.
3. Lukong KE, Elsliger MA, Chang Y, Richard C, Thomas G, Carey W, Tylki-Szymanska A, Czartoryska B, Buchholz T, Criado GR, Palmeri S, Pshezhetsky AV. Characterization of the sialidase molecular defects in sialidosis patients suggests the structural organization of the lysosomal multienzyme complex. Hum Mol Genet. 2000 Apr 12;9(7):1075-85. doi: 10.1093/hmg/9.7.1075. PMID: 10767332.
4. Naganawa Y, Itoh K, Shimmoto M, Takiguchi K, Doi H, Nishizawa Y, Kobayashi T, Kamei S, Lukong KE, Pshezhetsky AV, Sakuraba H. Molecular and structural studies of Japanese patients with sialidosis type 1. J Hum Genet. 2000;45(4):241-9. doi: 10.1007/s100380070034. PMID: 10944856.
5. Oohira T, Nagata N, Akaboshi I, Matsuda I, Naito S. The infantile form of sialidosis type II associated with congenital adrenal hyperplasia: possible linkage between HLA and the neuraminidase deficiency gene. Hum Genet. 1985;70(4):341-3. doi: 10.1007/BF00295374. PMID: 3874816.
6. Pattison S, Pankarican M, Rupar CA, Graham FL, Igdoura SA. Five novel mutations in the lysosomal sialidase gene (NEU1) in type II sialidosis patients and assessment of their impact on enzyme activity and intracellular targeting using adenovirus-mediated expression. Hum Mutat. 2004 Jan;23(1):32-9. doi: 10.1002/humu.10278. PMID: 14695530.
7. Penzel R, Uhl J, Kopitz J, Beck M, Otto HF, Cantz M. Splice donor site mutation in the lysosomal neuraminidase gene causing exon skipping and complete loss of enzyme activity in a sialidosis patient. FEBS Lett. 2001 Jul 20;501(2-3):135-8. doi: 10.1016/s0014-5793(01)02645-x. PMID: 11470272.
8. Sergi C, Penzel R, Uhl J, Zoubaa S, Dietrich H, Decker N, Rieger P, Kopitz J, Otto HF, Kiessling M, Cantz M. Prenatal diagnosis and fetal pathology in a Turkish family harboring a novel nonsense mutation in the lysosomal alpha-N-acetyl-neuraminidase (sialidase) gene. Hum Genet. 2001 Oct;109(4):421-8. doi: 10.1007/s004390100592. PMID: 11702224.
9. Seyrantepe V, Poupetova H, Froissart R, Zabot MT, Maire I, Pshezhetsky AV. Molecular pathology of NEU1 gene in sialidosis. Hum Mutat. 2003 Nov;22(5):343-52. doi: 10.1002/humu.10268. PMID: 14517945.
10. Ledvinová J, Poupĕtová H, Elleder M, Tichý J, Pĕnicková V, Harzer K. Sialidosis type I: first report in the Czech population of two siblings with cherry-red spot myoclonus syndrome but without sialyloligosacchariduria. J Inherit Metab Dis. 1994;17(1):118-9. doi: 10.1007/BF00735411. PMID: 8051919.
11. Uhl J, Penzel R, Sergi C, Kopitz J, Otto HF, Cantz M. Identification of a CTL4/Neu1 fusion transcript in a sialidosis patient. FEBS Lett. 2002 Jun 19;521(1-3):19-23. doi: 10.1016/s0014-5793(02)02748-5. PMID: 12067718.
12. Bonten E, van der Spoel A, Fornerod M, Grosveld G, d'Azzo A. Characterization of human lysosomal neuraminidase defines the molecular basis of the metabolic storage disorder sialidosis. Genes Dev. 1996 Dec 15;10(24):3156-69. doi: 10.1101/gad.10.24.3156. PMID: 8985184.
13. Lowden JA, O'Brien JS. Sialidosis: a review of human neuraminidase deficiency. Am J Hum Genet. 1979 Jan;31(1):1-18. PMID: 107795; PMCID: PMC1685665.
14. Sergi C, Beedgen B, Kopitz J, Zilow E, Zoubaa S, Otto HF, Cantz M, Linderkamp O. Refractory congenital ascites as a manifestation of neonatal sialidosis: clinical, biochemical and morphological studies in a newborn Syrian male infant. Am J Perinatol. 1999;16(3):133-41. doi: 10.1055/s-2007-993847. PMID: 10438195.
15. Lemyre E, Russo P, Melançon SB, Gagné R, Potier M, Lambert M. Clinical spectrum of infantile free sialic acid storage disease. Am J Med Genet. 1999 Feb 19;82(5):385-91. PMID: 10069709.
16. Loren DJ, Campos Y, d'Azzo A, Wyble L, Grange DK, Gilbert-Barness E, White FV, Hamvas A. Sialidosis presenting as severe nonimmune fetal hydrops is associated with two novel mutations in lysosomal alpha-neuraminidase. J Perinatol. 2005 Jul;25(7):491-4. doi: 10.1038/sj.jp.7211335. PMID: 15908988.
17. Lee BH, Kim YM, Kim JH, Kim GH, Lee BS, Kim CJ, Yoo HJ, Yoo HW. Histological, biochemical, and genetic characterization of early-onset fulminating sialidosis type 2 in a Korean neonate with hydrops fetalis. Brain Dev. 2014 Feb;36(2):171-5. doi: 10.1016/j.braindev.2013.01.012. Epub 2013 Feb 19. PMID: 23433491.
18. Tabardel Y, Soyeur D, Vivario E, Senterre J. Déficit primitif en neuraminidase à révélation anté-natale [Primary neuraminidase deficiency with prenatal disclosure]. Arch Fr Pediatr. 1989 Dec;46(10):737-40. French. PMID: 2697196.
19. Ahn JH, Kim AR, Lee C, Kim NKD, Kim NS, Park WY, Kim M, Youn J, Cho JW, Kim JS. Type 1 Sialidosis Patient With a Novel Deletion Mutation in the NEU1 Gene: Case Report and Literature Review. Cerebellum. 2019 Jun;18(3):659-664. doi: 10.1007/s12311-019-1005-2. PMID: 30635863.
20. Gultekin M, Bayramov R, Karaca C, Acer N. Sialidosis type I presenting with a novel mutation and advanced neuroimaging features. Neurosciences (Riyadh). 2018 Jan;23(1):57-61. doi: 10.17712/nsj.2018.1.20170328. PMID: 29455223.
21. Ranganath P, Sharma V, Danda S, Nandineni MR, Dalal AB. Novel mutations in the neuraminidase-1 (NEU1) gene in two patients of sialidosis in India. Indian J Med Res. 2012 Dec;136(6):1048-50. PMID: 23391804; PMCID: PMC3612311.
22. Sekijima Y, Nakamura K, Kishida D, Narita A, Adachi K, Ohno K, Nanba E, Ikeda S. Clinical and serial MRI findings of a sialidosis type I patient with a novel missense mutation in the NEU1 gene. Intern Med. 2013;52(1):119-24. doi: 10.2169/internalmedicine.52.8901. Epub 2013 Jan 1. PMID: 23291686.
23. Sobral I, Cachulo Mda L, Figueira J, Silva R. Sialidosis type I: ophthalmological findings. BMJ Case Rep. 2014 Oct 16;2014:bcr2014205871. doi: 10.1136/bcr-2014-205871. PMID: 25323282; PMCID: PMC4202095.
24. Canafoglia L, Robbiano A, Pareyson D, Panzica F, Nanetti L, Giovagnoli AR, Venerando A, Gellera C, Franceschetti S, Zara F. Expanding sialidosis spectrum by genome-wide screening: NEU1 mutations in adult-onset myoclonus. Neurology. 2014 Jun 3;82(22):2003-6. doi: 10.1212/WNL.0000000000000482. Epub 2014 May 7. PMID: 24808020.
25. Schene IF, Kalinina Ayuso V, de Sain-van der Velden M, van Gassen KL, Cuppen I, van Hasselt PM, Visser G. Pitfalls in Diagnosing Neuraminidase Deficiency: Psychosomatics and Normal Sialic Acid Excretion. JIMD Rep. 2016;25:9-13. doi: 10.1007/8904\_2015\_472. Epub 2015 Jul 5. PMID: 26141460; PMCID: PMC5059187.
26. Mütze U, Bürger F, Hoffmann J, Tegetmeyer H, Heichel J, Nickel P, Lemke JR, Syrbe S, Beblo S. Multigene panel next generation sequencing in a patient with cherry red macular spot: Identification of two novel mutations in NEU1 gene causing sialidosis type I associated with mild to unspecific biochemical and enzymatic findings. Mol Genet Metab Rep. 2016 Dec 1;10:1-4. doi: 10.1016/j.ymgmr.2016.11.004. PMID: 27942463; PMCID: PMC5137178.
27. Gowda VK, Srinivasan VM, Benakappa N, Benakappa A. Sialidosis Type 1 with a Novel Mutation in the Neuraminidase-1 (NEU1) Gene. Indian J Pediatr. 2017 May;84(5):403-404. doi: 10.1007/s12098-016-2286-9. Epub 2017 Jan 31. PMID: 28138907.
28. Aravindhan A, Veerapandiyan A, Earley C, Thulasi V, Kresge C, Kornitzer J. Child Neurology: Type 1 sialidosis due to a novel mutation in NEU1 gene. Neurology. 2018 Mar 27;90(13):622-624. doi: 10.1212/WNL.0000000000005209. PMID: 29581327.
29. Hu SC, Hung KL, Chen HJ, Lee WT. Seizure remission and improvement of neurological function in sialidosis with perampanel therapy. Epilepsy Behav Case Rep. 2018 Mar 12;10:32-34. doi: 10.1016/j.ebcr.2018.02.005. PMID: 29977792; PMCID: PMC6030028.
30. Mohammad AN, Bruno KA, Hines S, Atwal PS. Type 1 sialidosis presenting with ataxia, seizures and myoclonus with no visual involvement. Mol Genet Metab Rep. 2018 Jan 12;15:11-14. doi: 10.1016/j.ymgmr.2017.12.005. PMID: 30023283; PMCID: PMC6047061.
31. Cameron PD, Dubowitz V, Besley GT, Fensom AH. Sialic acid storage disease. Arch Dis Child. 1990 Mar;65(3):314-5. doi: 10.1136/adc.65.3.314. PMID: 2334213; PMCID: PMC1792249.
32. Cooper A, Sardharwalla IB, Thornley M, Ward KP. Infantile sialic acid storage disease in two siblings. J Inherit Metab Dis. 1988;11 Suppl 2:259-62. doi: 10.1007/BF01804252. PMID: 3141716.
33. Hale LP, van de Ven CJ, Wenger DA, Bradford WD, Kahler SG. Infantile sialic acid storage disease: a rare cause of cytoplasmic vacuolation in pediatric patients. Pediatr Pathol Lab Med. 1995 May-Jun;15(3):443-53. doi: 10.3109/15513819509026980. PMID: 8597831.
34. Paschke E, Trinkl G, Erwa W, Pavelka M, Mutz I, Roscher A. Infantile type of sialic acid storage disease with sialuria. Clin Genet. 1986 May;29(5):417-24. doi: 10.1111/j.1399-0004.1986.tb00514.x. PMID: 3742847.
35. Pueschel SM, O'Shea PA, Alroy J, Ambler MW, Dangond F, Daniel PF, Kolodny EH. Infantile sialic acid storage disease associated with renal disease. Pediatr Neurol. 1988 Jul-Aug;4(4):207-12. doi: 10.1016/0887-8994(88)90032-x. PMID: 3072006.
36. Schleutker J, Leppänen P, Månsson JE, Erikson A, Weissenbach J, Peltonen L, Aula P. Lysosomal free sialic acid storage disorders with different phenotypic presentations--infantile-form sialic acid storage disease and Salla disease--represent allelic disorders on 6q14-15. Am J Hum Genet. 1995
37. Kang E, Kim YM, Heo SH, Jung E, Kim KS, Yoo HJ, Kim EN, Kim CJ, Kim GH, Lee BH. Biochemical and molecular analyses of infantile sialic acid storage disease in a patient with nonimmune hydrops fetalis. Clin Chim Acta. 2018 Jul;482:199-202. doi: 10.1016/j.cca.2018.04.016. Epub 2018 Apr 11. PMID: 29654786.
38. Huang YZ, Lai SC, Lu CS, Weng YH, Chuang WL, Chen RS. Abnormal cortical excitability with preserved brainstem and spinal reflexes in sialidosis type I. Clin Neurophysiol. 2008 May;119(5):1042-50. doi: 10.1016/j.clinph.2008.01.023. Epub 2008 Mar 17. PMID: 18343720.
39. Young ID, Young EP, Mossman J, Fielder AR, Moore JR. Neuraminidase deficiency: case report and review of the phenotype. J Med Genet. 1987 May;24(5):283-90. doi: 10.1136/jmg.24.5.283. PMID: 3585942; PMCID: PMC1050052.
40. Arora V, Setia N, Dalal A, Vanaja MC, Gupta D, Razdan T, Phadke SR, Saxena R, Rohtagi A, Verma IC, Puri RD. Sialidosis type II: Expansion of phenotypic spectrum and identification of a common mutation in seven patients. Mol Genet Metab Rep. 2020 Jan 11;22:100561. doi: 10.1016/j.ymgmr.2019.100561. PMID: 31956508; PMCID: PMC6957780.
41. Lee YJ, Son SK, Park JH, Song JS, Cheon CK. NEU1 mutation in a Korean infant with type 2 sialidosis presenting as isolated fetal ascites. Pediatr Neonatol. 2015 Feb;56(1):68-9. doi: 10.1016/j.pedneo.2014.05.004. Epub 2014 Sep 12. PMID: 25223955.
42. Neeraja K, Holla VV, Prasad S, Surisetti BK, Rakesh K, Kamble N, Yadav R, Pal PK. Sialidosis Type I without a Cherry Red Spot- Is There a Genetic Basis? J Mov Disord. 2020 Oct 31. doi: 10.14802/jmd.20083. Epub ahead of print. PMID: 33121223.
43. Caciotti A, Di Rocco M, Filocamo M, Grossi S, Traverso F, d'Azzo A, Cavicchi C, Messeri A, Guerrini R, Zammarchi E, Donati MA, Morrone A. Type II sialidosis: review of the clinical spectrum and identification of a new splicing defect with chitotriosidase assessment in two patients. J Neurol. 2009 Nov;256(11):1911-5. doi: 10.1007/s00415-009-5213-4. Epub 2009 Jul 1. PMID: 19568825.
44. Godra A, Kim DU, D'Cruz C. Pathologic quiz case: a 5-day-old boy with hydrops fetalis. Mucolipidoses I (Sialidosis III). Arch Pathol Lab Med. 2003 Aug;127(8):1051-2. doi: 10.1043/1543-2165(2003)127<1051:PQCADB>2.0.CO;2. PMID: 12873188.
45. Chen CM, Lai SC, Chen IC, Hsu KC, Lyu RK, Ro LS, Chang HS. First report of two Taiwanese siblings with sialidosis type I: a 10-year follow-up study. J Neurol Sci. 2006 Aug 15;247(1):65-9. doi: 10.1016/j.jns.2006.03.013. Epub 2006 May 18. PMID: 16712870.
46. Steinman L, Tharp BR, Dorfman LJ, Forno LS, Sogg RL, Kelts KA, O'Brien JS. Peripheral neuropathy in the cherry-red spot-myoclonus syndrome (sialidosis type I). Ann Neurol. 1980 May;7(5):450-6. doi: 10.1002/ana.410070510. PMID: 6249183.
47. Daich Varela M, Zein WM, Toro C, Groden C, Johnston J, Huryn LA, d'Azzo A, Tifft CJ, FitzGibbon EJ. A sialidosis type I cohort and a quantitative approach to multimodal ophthalmic imaging of the macular cherry-red spot. Br J Ophthalmol. 2020 Aug 4:bjophthalmol-2020-316826. doi: 10.1136/bjophthalmol-2020-316826. Epub ahead of print. PMID: 32753397.
48. Palmeri S, Villanova M, Malandrini A, van Diggelen OP, Huijmans JG, Ceuterick C, Rufa A, DeFalco D, Ciacci G, Martin JJ, Guazzi G. Type I sialidosis: a clinical, biochemical and neuroradiological study. Eur Neurol. 2000;43(2):88-94. doi: 10.1159/000008141. PMID: 10686466.
49. Vieira de Rezende Pinto WB, Sgobbi de Souza PV, Pedroso JL, Barsottini OG. Variable phenotype and severity of sialidosis expressed in two siblings presenting with ataxia and macular cherry-red spots. J Clin Neurosci. 2013 Sep;20(9):1327-8. doi: 10.1016/j.jocn.2012.12.014. Epub 2013 Jul 16. PMID: 23870618.
50. Michalewska Z, Gajos A, Michalewski J, Nawrocki J, Pshezhetsky AV, Bogucki A. Spectral optical coherence tomography in a patient with type I sialidosis. Med Sci Monit. 2011 Oct;17(10):CS129-31. doi: 10.12659/msm.881971. PMID: 21959619; PMCID: PMC3539471.
51. Heroman JW, Rychwalski P, Barr CC. Cherry red spot in sialidosis (mucolipidosis type I). Arch Ophthalmol. 2008 Feb;126(2):270-1. doi: 10.1001/archophthalmol.2007.31. PMID: 18268224.
52. Rosenberg R, Halimi E, Mention-Mulliez K, Cuisset JM, Holder M, Defoort-Dhellemmes S. Five year follow-up of two sisters with type II sialidosis: systemic and ophthalmic findings including OCT analysis. J Pediatr Ophthalmol Strabismus. 2013 Jul 2;50 Online:e33-6. doi: 10.3928/01913913-20130625-02. PMID: 23819954.
53. Ganguly S, Gabani RU, Chakraborty S, Ganguly SB. Sialidosis type I (cherry red spot-myoclonus syndrome). J Indian Med Assoc. 2004 Mar;102(3):174-5. PMID: 15473282.
54. Kersten HM, Roxburgh RH, Danesh-Meyer HV, Hutchinson DO. Optical coherence tomography findings in a patient with type 1 sialidosis. J Clin Neurosci. 2016 Sep;31:199-201. doi: 10.1016/j.jocn.2016.02.015. Epub 2016 Apr 1. PMID: 27052257.
55. Coppola A, Ianniciello M, Vanli-Yavuz EN, Rossi S, Simonelli F, Castellotti B, Esposito M, Tozza S, Troisi S, Bellofatto M, Ugga L, Striano S, D'Amico A, Baykan B, Striano P, Bilo L. Diagnosis and Management of Type 1 Sialidosis: Clinical Insights from Long-Term Care of Four Unrelated Patients. Brain Sci. 2020 Aug 1;10(8):506. doi: 10.3390/brainsci10080506. PMID: 32752208; PMCID: PMC7465165.