**Supplementary Table S3**. Summary of descriptive characteristics of included lysosomal acid lipase deficiency articles and patients.

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| **STUDY** | **POPULATION CHARACTERISTICS** | **CLINICAL CHARACTERISTICS** | **DIAGNOSIS** |
| **Author, Year (Country)** | **Study design** | **Spectrum****of LAL-D** | **Sex** | **Age at onset / diagnostic / death (months)** | **Consangui-****nity** | **Clinical Manifestations and Comorbities** | **Laboratory findings** | **Tissue anatomic pathology** | **LAL activity / *LIPA* Mutation** |
| Akcoren et al, 1999(Turkey) | Case Report | CESD | Female | 42/ 42/n.r. | No | HSM | ET, HC, LH, HTG | PBF, BRC | <1% (b) / n.r. |
| Akki et al, 2018(Mexico) | Case Report | CESD | Male | 72/144/n.r. | n.r. | HM, OB | ET, HC, LH, HS | HLD, MVS, PBF, | 0% (b)/c.894G>A/c.894G>A |
| Al Essa et al,1988 (A)(Saudi Arabia) | Case Report | Infantile | Female | n.r./n.r. /n.r. | Yes | AD, HSM, FTT, D, V, ST | A, TR, ET, CA | BMV, HFC | 2% (b) (c)/ n.r. |
| Al Essa et al,1988 (B)(Saudi Arabia) | Case Report | Infantile | Male | 2/2/2 | n.r. | HSM, FTT | CA, ET | n.r. | <1% (c)/ n.r. |
| Al Essa et al,1988 (C)(Saudi Arabia) | Case Report | Infantile | Male | 3/3/6 | Yes | AD, HSM, FTT | ET | n.r. | 5%(c) / n.r. |
| Al Essa et al,1988 (D)(Saudi Arabia) | Case Report | Infantile | Female | 3/3/4 | Yes | AD, HSM, FTT, D, V, J | CA, ET, BVL | BMV | 6% (c) / n.r. |
| Anderson et al, 1999 (A) (United States) | Case Report | Infantile | Male | 2/2/4 | No | HM | AC | BMV | 4% (b)Exon 4 skipped / undetermined |
| Anderson et al, 1999 (B) (United States) | Case Report | Infantile | Male | 0/3/4 | No | n.r. | BVL, AC | BMVHS, BPF | 3%(b) 1% (c)c.347G>A/ c.684delT |
| Anderson et al, 1999 (C) (United States) | Case Report | Infantile | Female | 2/3/3 | No | HM, D, V | n.r. | n.r | 0% (c)c.594-595insT/c.193C>T |
| Anderson et al, 1999 (D) (United States) | Case Report | CESD | Male | 36/36/n.r. | No | HM | n.r. | BMVHL, MVS | 1,2%(c)c.894G>a/c.894G>a |
| Arbisser et al,1978 (United States) | Case Report | CESD | Male | 132/ n.r./n.r. | Yes | HSM, UH | ET, HTG, HC | HLD | 0% (c) / n.r. |
| Beaudet et al, 1977 ( United States) | Case Report | CESD | Female | 24/n.r./n.r. | No | HSM, FTT | HC, CA | BMVHLDDU | 6% (b) / n.r. |
| Ben Hassine et al, 2016(Tunisia) | Case Report | Infantile | Female | 3/3/4.5 | Yes | HSM, FTT, | A, DYS | n.r. | LAL-D (b) / n.r. |
| Ben-Haroush et al, 2003 (Israel) | Case Report | Infantile | Female | 0/1/n.r. | n.r. | HM, ABFetal ascites | CA, BVL | n.r. | 2%(b) / n.r. |
| Benevides et al, 2018 (A) (Brazil) | Case Serie | CESD | Male | 108/125/n.r. | No | HM, AP | HC, LH | n.r. | 20% (b)c.266T>C/wt |
| Benevides et al, 2018 (B) (Brazil) | Case Serie | CESD | Female | 72/84/n.r. | n.r. | HM | ET, HC, LH, HTG | n.r. | 0% (b)c.894G>A/c.894G>A |
| Benevides et al, 2018 (C) (Brazil) | Case Serie | CESD | Male | 36/36/n.r. | n.r. | HM | ET, HC, LH, HTG | HLD | 0%/c.894G>A/c.894G>A |
| Benevides et al, 2018 (D) (Brazil) | Case Serie | Infantile | Male | 4/36/n.r. | Yes | HM, D, FTT, AS | ET, HC, LH, HTG, AC | MVS | 0%/c.266T>C/c.266T>C |
| Benevides et al, 2018 (E) (Brazil) | Case Serie | CESD | Male | 96/108/n.r. | n.r. | HM | ET, HC, HTG, LH | n.r. | 0%/c.266T>C/wt |
| Benevides et al, 2018 (F) (Brazil) | Case Serie | CESD | Female | 72/72/n.r. | n.r. | AP | ET, HC, HTG, LH | n.r. | 30%/c.67G>A/wt |
| Benevides et al, 2018 (G) (Brazil) | Case Serie | CESD | Male | 24/120/n.r. | n.r. | HM, AP | HC, LH | G, PBF, HS, Kv | 0%c.894G>A/c.894GA |
| Bernstein et al, 2014 (United States) | Case Report | CESD | Male | 20/24/n.r. | n.r. | HM, D, V | ET, HC | HS, PBF | LAL-D (b) / c.894G>A/c.297\_311del |
| Bindu et al,2007(India) | CaseReport | CESD | Male | 8/48/n.r. | Yes | AI, NS, cataract, HSM, AD, FTT | A, HTG, HC, AC, BVL | FC | 46,7% (b) / n.r. |
| Bindu et al,2007(India) | CaseReport | CESD | Male | 1/22/n.r. | Yes | AI, NS, HM, V, FTT | AC | n.r. | 50% (b) / n.r. |
| Boldrini et al, 2004 (A) (Italy) | Case Report | Infantile | Male | 2/2/5 | n.r | D, V, FTT | AC | DU | 0%(b)(c) / n.r. |
| Boldrini et al, 2004 (B) (Italy) | Case Report | Infantile | Female | 60/60/n.r. | n.r | HSM, D | AC, DYS | MVS, PBF, kV | 0%(b)(c) / n.r. |
| Boldrini et al, 2004 (C) (Italy) | Case Report | Infantile | Male | 60/60/n.r. | n.r | HSM, D | AC | MVS, PBF, C, kV | 0%(b)(c) / n.r. |
| Boldrini et al, 2004 (D) (Italy) | Case Report | CESD | Female | 144/144/n.r. | n.r | HSM | DYS, HSi | HS,MVS, PBF, G, kV | LAL-D (b)(c) / n.r. |
| Boldrini et al, 2004 (E) (Italy) | Case Report | CESD | Male | 144/144/n.r. | n.r | HSM | DYS, HSi | HS,MVS, PBF, G, kV | LAL-D (b)(c) / n.r. |
| Bona et al, 1988 (United Kingdom) | Case Report | Infantile | Female | 1/3/n.r. | n.r. | HSM, D, V, IH | A, AC, ET, HC, HTG, BVL, ALF | n.r. | 16%(b), 11% (c) / n.r. |
| Botero et al, 2018 (Columbia) | Case Report | CESD | Male | 72/168/n.r. | No | HM, Patent ductus arteriosus | ET, HTG, HC, HSi | MVS, PBF | n.r./c.894G>A/c.894G>A |
| Browme et al, 2003 (Australia) | Case Report | Infantile | Male | 1/2/2 | Yes | FTT, HSM, D, hypotonia | A, TR, AFL | BMVHL, MVS | 0% (b)/ n.r. |
| Cagle et al, 1986 (United States) | Case Report | CESD | Female | 24/132/n.r. | No | HSM | AC, ET, HTG, HC | FCDUHL, kV | 5%(c) / n.r. |
| Camelo et al, 2017 (Brazil) | Case Report | Infantile | Female | 0/0/n.r. | Yes | HM, AD, FTT, food allergy | ET, HTG, HC | n.r. | n.r. / c.266T>C/c.266T>C |
| Carbajal et al 2016 (A)(Mexico) | Case Report | Late-onset | Male | 57/57/n.r. | Yes | HSM, AD, J, cardiomyopathy | ET, HTG, HC | HS, MVS, PBF, kV | 0%(a)/c.894G>A/c.894G>A |
| Carbajal et al 2016 (B) (Mexico) | Case Report | CESD | Female | 181/181/n.r. | Yes | HM | HTG, HC | HS, MVS, PBF, kV | 0% (a)/c.894G>A/c.894G>A |
| Cansever et al,1999 (Turkey) | Case Report | Infantile | Female | 1/1/n.r. | Yes | HSM, AD, FTT | AC, ET, HTG, HC | n.r. | 5,4%(a)/homozygous (c.493\_494insC) |
| Chabchoub et al, 2020 (Tunisia) | Case Report | Infantile | Female | 21/21/n.r. | n.r. | AD, HL, HSM | ET, HC, HTG, LH | BMV, HFCMVS, PBF | 16,6%(b)exon 9: c.966G>C |
| Chen et al, 2017 (Canada) | Case Report | CESD | Female | 96/96/n.r. | No | AP, HSM | ET, HC, LH | MVS, PBF | 16%(a)c.684delT/c.894G>A |
| Cohen et al, 2019 (B) (United States) | Case Report | Infantile | Female | n.r./ 2 /n.r. | n.r. | HSM, HL,D | A, TR, ET, HTG, HC, LH | Not performed | 0% (n.r.) /c.656 T>G /c.656T>G |
| Curiati et al, 2018 (A) (Brazil) | Case Report | CESD | Female | 36/48/108 | No | HSM, D, FTT | HTG, HG, LH | MVS, HL, kV | 1,83% (a) / n.r. |
| Curiati et al, 2018 (B) (Brazil) | Case Report | CESD | Male | 6/48/n.r. | No | HSM | ET, HC, HTG, LH | HL, Kvdeformed villus | 2,35% (a) / n.r. |
| Curiati et al, 2018 (C) (Brazil) | Case Report | CESD | Male | n.r./60/n.r | No | Asymptomatic, Familiar Screening | HM | Not performed | 0% (a) / n.r. |
| Curiati et al, 2018 (D) (Brazil) | Case Report | CESD | Male | 36/36/n.r. | No | D, Familiar Screening | HTG, LH | Not performed | 0% (a) / n.r. |
| Curiati et al, 2018 (E) (Brazil) | Case Report | Infantile | Male | 0/4/8 | No | I, HSM, FTT, HL | A, TR, ALF, ET, HTG, HC, LH | MVS, PBF | 8,75% (a) / c.477delT/ c.822+37\_38insC |
| D`Agostino et al, 1988 (A) (United States) | Case Report | CESD | Female | 120/120/n.r. | No | HSM, AP | HC, HGT | HL, PBF, kV | 1,3%(b) / n.r. |
| D`Agostino et al, 1988 (B) (United States) | Case Report | CESD | Female | 144/144/n.r. | No | HM | HC | n.r. | 1,7%(b) / n.r. |
| D`Agostino et al, 1988 (C) (United States) | Case Report | CESD | Female | 1/86/n.r. | Yes | HSM, D | ET, HC, HTG, LH | PBF, kV, HL, BRC | 0%(b) / n.r. |
| D`Agostino et al, 1988 (D) (United States) | Case Report | CESD | Male | 132/132/n.r. | No | HM | HC, LH | n.r. | 3,5%(b) / n.r. |
| Dalgic et al, 2006 (Turkey) | Case Report | CESD | Male | 24/24/n.r. | n.r. | HSM, AD | ET, HC, HTG, LH | HS,MVS, PBF, BRC | 1% (b) / n.r. |
| De Las Heras et al, 2017 (Spain) | Case Report | Infantile | Male | 0.5/2/n.r. | Yes | S, AD, D, V, FTT | A, ET, HTG, BVL | n.r. | 0%(a)/ homo-zygous located in intron 6 |
| Decarlis et al, 2009 (Italy) | Case Report | CESD | Female | 96/156/n.r. | No | HSM, | ET, HTG, HC, LH, HSi | n.r. | 7%(b), 16%(c) / n.r. |
| Desai et al, 1986 (United States) | Case Report | CESD | Female | 24/108/n.r. | No | HSM, FTT, | ET, HC, HTG | HS,G,PBF,BRC,kDU | 4%(b) / n.r. |
| Di Bisceglie et al, 1989 (A) (United States) | Case Report | CESD | Female | 36/144/n.r. | n.r. | HSM,D,V | ET, HC, HTG | HS,M VS, PBF, BRC, kV | 0,1% (c) / n.r. |
| Di Bisceglie et al, 1989 (B) (United States) | Case Report | CESD | Female | 60/60/n.r. | n.r. | HM | ET, HC,HTG, LH | HS,MVS, PBF | 2,5%(c) / n.r. |
| Dutton et al, 1985 (United States) | Case Report | Infantile | Female | 2/9.5/n.r. | No | HSM, IH,V, NS, FTT, AD | AC | n.r. | 6%(b), 5%(c) / n.r. |
| Edelstein et al, 1988 (United States) | Case Report | CESD | Female | 6/120/n.r. | Yes | HSM, EV, PTH, AP, D, Splenic abscess  | TR, ET, HTG, HC | MVS, PBF, C | 16% (c) / n.r. |
| Ellis et al, 1976 (Pakistan) | Case Report | Infantile | Male | 5/5/5 | No | HSM, V, FTT | HSi, AC, A, HTG | BMVLiver: HS | 0%(b) / n.r. |
| Elsayed et al, 2016 (A)(Egypt) | Case Report | Infantile | Male | 1/2.5/n.r. | Yes | HSM, AD, FTT, HL | A, TR, HTG | HFC | n.r. /c.G969A/ c.G969A |
| Elsayed et al, 2016 (B) (Egypt) | Case Report | Infantile | Female | 3/3/n.r. | Yes | HSM, FTT, HL | A, TR, HTG | HFC | n.r./c.438delC/c.438delC |
| Elsayed et al, 2016 (C) (Egypt) | Case Report | Infantile | Male | 2.5/ 3/n.r. | Yes | HSM, AD, FTT, HL | A, TR, HTG | n.r. | n.r./c.G9694/c.G9694 |
| Fasano et al, 2012 (A) (Italy) | Case Report | Infantile | Male | 2/2/6 | Yes | HSM, AD, D, ST, FTT | A, ET, AC | BMV | 5,5%(c)c.229+1G>A/ c.229+1G>A |
| Fasano et al, 2012 (B) (Italy) | Case Report | Infantile | Female | 2/2/5 | No | HSM, AD, FTT | A, ET, AC | BMV | 1,7% (c)c.796G>T /c.796G>T |
| Fasano et al, 2012 (C) (Italy) | Case Report | Infantile | Female | 4/4/4 | Yes | HSM, AD ,D,V, FTT | AC | n.r. | LAL deficiency (b)c.419G>A / c.419G>A |
| Fasano et al, 2012 (D) (Italy) | Case Report | CESD | Male | 48/120/n.r. | Yes | HSM, AD | ET, HTG, HC | HS, HL, PBF | 6,4% (c)c.894G>A /c.894G>A |
| Fasano et al, 2012 (E) (Italy) | Case Report | CESD | Female | 36/36/n.r. | No | HM | ET | n.r. | 8%(c)c.894G>A / c.894G>A |
| Fasano et al, 2012 (F) (Italy) | Case Report | CESD | Male | 84/84/n.r. | n.r. | HM | HC | HS | n.r./c.894G>A / c.419G>A |
| Fasano et al, 2012 (G) (Italy) | Case Report | CESD | Male | 48/48/n.r. | No | HM | ET, HC | n.r. | 2,3% (c)c.894G>A/ c1883C>T |
| Fasano et al, 2012 (H) (Italy) | Case Report | CESD | Male | 84/84/n.r. | No | HM | ET, HC | n.r. | 1,8% (b)c.894G>A/ c102G>A |
| Ferry et al, 1991 (United States) | Case Report | CESD | Female | 72/72/n.r. | n.r. | HSM | ET, HC, HTG, LH | HL, HS, PBF, BRC | 6,8%(b) / n.r. |
| Freudenberg, 2013 (Germany) | Case Report | CESD | Male | 60/156/n.r. | n.r. | Asymptomatic | ET, HC | HL, PBF, BRC | n.r./c.831G>A/c.831G>A |
| Fuyijama et al,1986 (Japan) | Case Report | Infantile | Female | 1/n.r./4 | Yes | HSM, UH, D,V | A, AC | n.r. | 2,8% (c)c.169G>C |
| Gomez-Najera, 2015 (United States) | Case Report | Infantile | Female | 2.5/5/5 | No | HSM, J, FTT | AC, A, T, ALF, BVL, ET, HC, HTG | n.r. | n.r. /c.894G>C / c.1024G>A |
| Gopakumar et al, 2017 (India) | Case Report | Infantile | Male | 1/ 2.5/n.r. | No | UH, FTT, AD | AC, HTG | BMV | 2,75% (b)c.1180\_1184del |
| Haller et al, 2010 (A) (United Kingdom) | Case Report | CESD | Male | 12/48/n.r. | n.r. | IF, AP, ST | HC, Gallbladder dysfunction | MVSDU | LAL-D (b)(c)/ Compound heterozygous |
| Haller et al, 2010 (B) (United Kingdom) | Case Report | CESD | Female | 156/168/n.r. | n.r. | HSM, AP, NS | HTG, HC, Gallbladder dysfunction | n.r. | LAL-D (b)(c) /Compound heterozygous |
| Haller et al, 2010 (C) (United Kingdom) | Case Report | CESD | Male | 72/72/n.r. | n.r. | AP, PHThepatic cirrhosis | ET, ALF Gallbladder dysfunction | n.r. | LAL-D (b)(c)/Compound heterozygous |
| Himmes et al, 2016 (A) (United States) | Case Report | CESD | Female | 96/96/n.r. | n.r. | IF | ET, HC | HS, PBF, BRC | n.r./c.894G>A |
| Himmes et al, 2016 (B) (United States) | Case Report | CESD | Female | 192/192/n.r. | n.r. | S | ET, HC | HS,PBF | n.r. / c.920C>A /c.1055\_1057delacg |
| Hoeg et al, 1984 (A) (United States) | Case Report | CESD | Male | 4/23/n.r. | n.r. | HSM | ET, HTG | n.r. | 3% (c) / n.r. |
| Hoeg et al, 1984 (B) (United States) | Case Report | Infantile | Female | 4/n.r./n.r. | n.r. | IF, aganglionisis | ET | n.r. | 3% (c) / n.r. |
| Ikari et al,2018 (Japan) | Case Report | Infantile | Female | 1/4/4 | Yes | HSM, AD, D, V, | AC, A, TR, HTG, | BMV | 7% (n.r.) /c.169C>G and pTyr22Ter( homozygous) |
| Julien et al, 2016 (United States) | Case Report | Infantile | Female | 0.5/0.5/n.r. | n.r. | HSM, D, V, FTT | A, TR, AC,decreased absolute CD4 CD8/CD19 cell | BMV | 0% (b)c.658C>T/p.220S |
| Karmaker et al, 2018 (Bangladesh) | Case Report | CESD | Female | 80/192/n.r. | Yes | HM, D,V,AP, NS,PHT,FTT, EV | A, HGT, ALF | Chronic Hepatitis | LAL-D (n.r.)/ n.r. |
| Katruria et al,2012 (India) | Case Report | Infantile | Male | 1 /2.5 / 3 | No | HSM, AD, AS, J, FTT, PHT, ST | AC, A, HTG | kV | 0%(b) / n.r. |
| Kelly et Al, 1985 (United States) | Case Report | CESD | Female | 23/23/n.r. | No | IF, HSM, AD / aganglionisis | HC, LH, HTG | BMVG, HLD, MVS, kV, PBF, BRC | 0,7% ( b e c) / n.r. |
| Kikuchi et al, 1991 (Japan) | Case Report | Infantile | Male | 1/2/6 | Yes | HSM, D, ST, FFT | AC, A | BMV Liver: HL, kV, PBF | 1,1% (b) / n.r. |
| Kim et al, 2017 (Korea) | Case Report | CESD | Male | 36/72/n.r. | n.r. | NS, HM, ADHypertension, hypercalcemiaglycogen storage disease | ET, HC, LH, HSi | HLD,MVS, kV, BRC | 3,8% (b)/ c.530C>T/c.530C>T |
| Klima et al, 1993 (Germany) | Case Report | CESD | Male | 60/120/n.r. | No | HSM | ET, HC, LH, HTG | HLD, MVS, kV | 2% (b), 9%(c)/Deletion of 72 bp exon from the mRNA |
| Kostner et al, 1985 (Austria) | Case Report | Infantile | N.r. | 48/48/n.r. | n.r. | IF, rickets,HM | HC, HTG | HLD, HS,C | LAL-D (b)/n.r. |
| Krause et al, 2018 ( Israel) | Case Report | Infantile | Female | n.r./4/n.r. | n.r. | FTT, HSM, AD, D | A, ET, DYS | n.r. | LAL-D (a)/Homozygous mutation in LIPA |
| Krivit et al, 2000 (A) (United States) | Case Report | Infantile | Male | 1/n.r./3 | No | HM, D, FTT | AC, BVL | Autopsy: Lipid storage in multiples organs | LAL-D (b)(c)c.347G>A/ stop condon; 724delT |
| Krivit et al, 2000 (B) (United States) | Case Report | Infantile | Female | 1/6/n.r. | No | HM, D, FTT | AC | HLD, PBF, kV | 0% (b)/c.347G>A/ stop condon; 724delT |
| Kucukcongar Yavas, 2017 (Turkey) | Case Report | Infantile | Female | 2/2/3 | Yes | FTT, D, V, HSM, HL | A, TR, HTG | HFC | 28% (b)/c.260G>T |
| Kuloglu, 2019 (A) (Turkey) | Cross-Sectional | CESD | Male | 60/180 | n.r. | FTT | ET, HC, HSi | n.r. | < 5% (b) / n.r. |
| Kuloglu, 2019 (B) (Turkey) | Cross-Sectional | CESD | Female | 72/75/n.r. | n.r. | Asymptomatic | ET, HC, HSi | MSV, PBF, PI | < 5% (b) / n.r. |
| Kuranobu et al, 2015 (Japan) | Case Report | CESD | Male | 132/132 | n.r. | HSM | ET, HC, HTG | MSV, PBF, kV | 11,7% (a)c.607G>C/c.791T>C |
| Lazzara et al, 2019 (United States) | Case Report | Infantile | Male | 0/6/n.r. | n.r. | AD, FTT, V, HSMfood allergy, constipation | A, ET, AC, HSi | n.r. | 26,7%(b)/c.531–2A>G/c.684del |
| Lee et al, 2011 (United States) | Case Report | Infantile | Male | 1.5/1.5/3 | No | HSM, AD, D,V, FTT, AI | AC, ALF | n.r. | n.r. / c.428delA |
| Leone et al, 1993 (Italy) | Case Report | CESD | Male | 19/48/n.r. | n.r. | AD, HSM | ET, HC, HTG, AC | HS,MVS, PBF | 16%(b) / n.r. |
| Limbach et al, 2003 (Germany) | Case Report | CESD | Male | 24/84/n.r. | n.r. | HM, AP | ET, HC | PBF | 11,8%(b) /Gly245→Stop mutation /Gly290→Arg |
| Linpinski et al, 2018 (A) (Poland) | Case Report | CESD | Female | 60 /120/n.r. | n.r. | HM, AP | HC, HTG | HLD, kV, BRC,C | 14,2% (b) / n.r. |
| Linpinski et al, 2018 (B) (Poland) | Case Report | CESD | Male | 60/ 72/n.r. | n.r. | HSM | ET, HC, HTG | HLD,PBF, kV, BRC | 6% (b) / n.r. |
| Linpinski et al, 2018 (C) (Poland) | Case Report | CESD | Male | 60/72/n.r. | n.r. | HSMgastric polyp | ET, HC, HTG | HLD, kV, BRC,C | 30,3% (b) / n.r. |
| Linpinski et al, 2018 (D) (Poland) | Case Report | CESD | Male | 6/24/n.r. | n.r. | HSM,pulmonary tuberculosis,agenesis of the left kidney | ET, HC | HLD, PBF, kV, BRC | 28,4% (b) / n.r. |
| Linpinski et al, 2018 (E) (Poland) | Case Report | CESD | Male | 132/168/n.r. | n.r. | HSM | - | HLD | 25,7% (b) / n.r. |
| Linpinski et al, 2018 (F) (Poland) | Case Report | CESD | Male | 178/156/n.r. | n.r. | HM | HG | n.r. | 1,93% (b) / n.r. |
| Linpinski et al, 2018 (G) (Poland) | Case Report | CESD | Female | 18/30/n.r. | n.r. | HM | ET, HC, HTG, LH | HLD,PBF, kV, BRC | 3,98% (b)/c.894G>A/c.894G>A |
| Linpinski et al, 2018 (H) (Poland) | Case Report | CESD | Female | 24/24/n.r. | n.r. | HM, diabetes mellitus type 1 | HC, HTG | n.r. | 4,24% (b)/c.894G>A/c.894G>A |
| Linpinski et al, 2018 (I) (Poland) | Case Report | CESD | Male | 24/120/n.r. | n.r. | HM | ET, HC, HTG, LH | HLD,PBF | 5% (b)/c.894G>A/c.894G>A |
| Linpinski et al, 2018 (J) (Poland) | Case Report | CESD | Male | 4/120/n.r. | n.r. | HM | ET, HC, HTG, LH | n.r. | 2,46% (b)c.538+5G>A/c.894G>A |
| Linpinski et al, 2018 (K) (Poland) | Case Report | CESD | Male | 120/132/n.r. | n.r. | HM | ET, HC, HTG, LH | PBF, kV | 3,11% (b) / n.r. |
| Linpinski et al, 2018 (L) (Poland) | Case Report | CESD | Female | 48/54/n.r. | n.r. | HSM | ET, HC, HTG, LH | n.r. | 2,94% (b)c.538+5G>A/c.894G>A |
| Linpinski et al, 2018 (M) (Poland) | Case Report | CESD | Female | 24/96/n.r. | n.r. | HM | ET, HC, HTG, LH | kV | 3,67% (b)c.309C>A/c.894G>A |
| Linpinski et al, 2018 (N) (Poland) | Case Report | CESD | Male | 24/108/n.r. | n.r. | HM, Gilbert’s syndrome | ET, HC, HTG, LH | HLD | 4,24% (b)c.894G>A/c.894G>A |
| Linpinski et al, 2018 (O)(Poland) | Case Report | CESD | Male | 84/120/n.r. | n.r. | HM | ET, HC, HTG, LH | HS, PBF | 5,54% (b) / n.r. |
| Linpinski et al, 2018 (P) (Poland) | Case Report | CESD | Male | 60/96/n.r. | n.r. | HSM | ET, HC, HTG, LH | HLD,PBF | 0,99% (b) / n.r.c.386A>C/c.894G>A |
| Linpinski et al, 2018 (Q) (Poland) | Case Report | CESD | Male | 84/84/n.r. | n.r. | HSM | ET, HC, HTG, LH | HLD | 1,6% (b)c.386A>C/c.894G>A |
| Linpinski et al, 2018 (R) (Poland) | Case Report | CESD | Male | 120/132/n.r. | n.r. | HSM | ET, LH | MVS,C | 2,77% (b) / n.r. |
| Linpinski et al, 2018 (S) (Poland) | Case Report | CESD | Male | 12/24/n.r. | n.r. | HSM | HC, HTG | HLD, kV | 15,4% (b) / n.r. |
| Linpinski et al, 2020 (Poland) | Case Report | CESD | Female | 24/36/n.r. | No | HSM, abdominal lymphadenopathy | ET, HC, HTG, LH | Lipidic storage in histiocytes | 1,26% (b)c.309C>A/c.894G>A |
| Longui et al, 1988 (Italy) | Case Report | CESD | Male | 60/96/n.r. | No | HSM, SH | HC, LH, HTG | HS, PBF | 3,8% (c) / n.r. |
| Maciejko et al, 2017 (A) (United States) | Case Report | CESD | Male | 48/132/n.r. | No | HM, FTT | ET, HC, HTG, LH | HS,MVS, PBF | 0%(a) LAL-D (b) / c.894G.A/ c.428+1G>A |
| Maciejko et al, 2017 (B) (United States) | Case Report | CESD | Male | n.r./204/n.r. | No | Gilbert’s syndrome | ET, HC, HTG, LH | n.r. | 0%(a), LAL deficiency (b)/c.894G.A/ c.428+1G>A |
| Maciejko et al, 2017 (C) (United States) | Case Report | CESD | Male | n.r./168/n.r. | No | Tuberous xanthomas | ET, HC, HTG, LH | n.r. | 0%(a), LAL-D (b)/c.894G.A/ c.428+1G>A |
| Maciejko et al, 2017 (D) (United States) | Case Report | CESD | Male | n.r./108/n.r. | No | Tuberous xanthomas | ET, HC, HTG, LH | n.r. | 0%(a), LAL-D (b)c.894G.A/c.428+1G>A |
| Mahdi et al, 1991 (Saudi Arabia) | Case Report | Infantile | Male | 1/2/4 | Yes | HSM, AD | ET, AC | BMV | 12%(c) / n.r. |
| Mayatepec et al, 1999 (Germany) | Case Report | Infantile | Female | 0/2/3 | Yes | HSM, AD, D, ST, V, FTT | A, TR,ALF, ETAC | HLD | 0% (b)(c) / n.r. |
| McCoy et al, 1991 (Canada) | Case Report | CESD | Male | 36/156 | n.r. | HSM | HC, LH, HTG | HLD | LAL-D (b) / n.r. |
| Meyers et al, 1985 (United States) | Case Report | Infantile | Male | 1.5/6/n.r. | n.r. | HM, D, ST,V, FTT | ET, AC | HLDDU | 1,8% (c) / n.r. |
| Michels et al,1969 (United States) | Case Report | CESD | Female | 24/96/n.r. | n.r. | HSM, SH, FTT, pulmonary symptoms, cerebrovascular accident | HC | C, kV | LAL-D (b) / n.r. |
| Mitsudo et al, 1989(United States) | Case Report | Infantile | Female | 1.5 / 2 /3 | n.r. | HSM | A, TR, HSi, HTG, AC, ALF, | HS, kV | LAL-D (c) / n.r. |
| Navarro et al, 1992 (Spain) | Case Report | CESD | Male | 24/48/n.r. | No | HSM, AD, FTT | ET, HTG | BMVHLD, PBF, kV | 2,7% (c) / n.r. |
| Nchimi et al, 2003 (Belgium) | Case Report | Infantile | Male | 1/1/4 | n.r. | D,V, AD, HM, Intestinal intussusception | AC, HSi | n.r. | LAL-D (c) / n.r. |
| Olga et al, 2017 (Russia) | Case Report | CESD | Female | 10/36/n.r. | Yes | HSM, PHT | ET, HC, HTG, HSi | n.r. | LAL-D (b) / n.r. |
| Orme et al, 1970 (England) | Case Report | Infantile | Female | 24/54/n.r. | n.r. | HM, AD | n.r. | BMVG, HS | 0% (b) / n.r. |
| Pagani et al, 1994 (Italy) | Case Report | CESD | Female | 18/108/n.r. | Yes | HM | ET, HTG | BRC | 3% (c)LIPA mRNA mutation |
| Pagani et al, 1998 (A) (Italy) | Case Report | Infantile | Male | 1/n.r./8 | n.r. | HM, D | AC, FTT | n.r. | LAL-D (b)/c.1012A>T/ c.1012A>T |
| Pagani et al, 1998 (B) (Italy) | Case Report | CESD | Female | 1/8/n.r. | n.r. | HM, D | AC, ET, FTT | BRC, C | LAL-D (b)/ c.903C>T |
| Pagani et al, 1998 (C) (Italy) | Case Report | CESD | n.r. | 72/n.r. /n.r. | n.r. | HM | ET, HC | PBF, kV | LAL-D (b)c.294C>G / c.894G>A |
| Pisciotta, 2009 (A) (Italy) | Case Report | CESD | Female | n.r./108 | No | HM | ET, HC, HCT | HS, PBF, kV, BRC | 5% (b)/c.652 C>T / c.894 G>A |
| Pisciotta, 2009 (B) (Italy) | Case Report | CESD | Female | n.r./108 | No | HM | ET, HC, HTG | n.r. | 5% (b)c.652 C>T / c.894 G>A |
| Pisciotta, 2017 (A) (Italy) | Case Report | CESD | Male | 60/n.r. /n.r. | n.r. | HSM | ET, DYS, HSi | n.r. | 1,250% (b)c652C>T /c.881T>C |
| Pisciotta, 2017 (B) (Italy) | Case Report | CESD | Male | 108/n.r. /n.r. | n.r. | HSM | ET, DYS, HSi | PBF | 1,250% (b)c.883C>T/ c.894G>A |
| Pisciotta, 2017 (C) (Italy) | Case Report | CESD | Male | 156/n.r. /n.r. | n.r. | Asymptomatic | ET, DYS, HSi | PBF | 2,50% (b)c.894G>A/ c.1033G>A |
| Pisciotta, 2017 (D) (Italy) | Case Report | CESD | Male | 36/n.r. /n.r. | n.r. | HM | ET, DYS, HSi | n.r. | 2,50% (b)c.894G>A/ c.1033G>A |
| Pisciotta, 2017 (E) (Italy) | Case Report | CESD | Male | 72/n.r. /n.r. | n.r. | HSM | ET, DYS, HSi | MVS | 3,75% (b)c.894G>A/ c.894G>A |
| Pisciotta, 2017 (F) (Italy) | Case Report | CESD | Male | 24/n.r. /n.r. | n.r. | HSM | ET, DYS, HSi | PBF | 3,75% (b)c.894G>A/ c.894G>A |
| Pisciotta, 2017 (G) (Italy) | Case Report | CESD | Male | 24/n.r. /n.r. | n.r. | HSM | ET, DYS, HSi | MVS, PBF | 2,50% (b)c.863C>T/ c.863C>T |
| Pisciotta, 2017 (H) (Italy) | Case Report | CESD | Female | 24/n.r. /n.r. | n.r. | HSM | ET, DYS, HSi | n.r. | 6,6% (b)c.894G>A/ c.1033G>A |
| Pisciotta, 2017 (I) (Italy) | Case Report | CESD | Female | 84/n.r. /n.r. | n.r. | HM | ET, DYS | MVS | 2,50% (b)/c.894G>A/ c.894G>A |
| Pisciotta, 2017 (J) (Italy) | Case Report | CESD | Female | 24/n.r. /n.r. | n.r. | HM | ET, DYS, HSi | HS | 3,2% (b)c.894G>A/ c.894G>A |
| Pisciotta, 2017 (K) (Italy) | Case Report | CESD | Male | 48/n.r. /n.r. | n.r. | HM, AI | ET, DYS, HSi | n.r. | 2,8% (b)c.419G>A/c.894G>A |
| Pisciotta, 2017 (L) (Italy) | Case Report | CESD | Male | 36/n.r. /n.r. | n.r. | HM | ET, DYS, HSi | n.r. | 17,6% (b)c.894G>A/c.1024G>A |
| Pisciotta, 2017 (M) (Italy) | Case Report | CESD | Male | 12/n.r. /n.r. | n.r. | HM | ET, DYS, HSi | HS, PBF | 0% (b) c.229+3A>C/c.229+3A>C |
| Pisciotta, 2017 (N) (Italy) | Case Report | CESD | Female | 36/n.r. /n.r. | n.r. | HM | ET, DYS, HSi | n.r. | 0% (b)c.796G>T/c.894G>A |
| Poinsot et al, 2016 (A) | Case Report | CESD | Male | n.r./ 103/n.r. | No | HM, AP, V, fever | ET, HC, LH, | MVS, PBF, kV | 6,25% (a)c.894G>A/c.894G>A |
| Poinsot et al, 2016 (B) | Case Report | CESD | Female | n.r./ 127/n.r. | No | HM, AP, V | ET HC, LH, HTG | MVS, PBF, kV | 0% (a)c.894G>A/c.894G>A |
| Poinsot et al, 2016 (C) | Case Report | CESD | Male | n.r./ 132/n.r. | No | AP, Jasthenia | ET, HC, LH, | MVS, PBF, kV | 0% (a)c.894G>A/c.398delC |
| Poinsot et al, 2016 (D) | Case Report | CESD | Female | n.r./ 157/n.r. | No | AP,V,J,asthenia | ET, HC, LH, | MVS, PBF, kV | 0% (a)c.894G>A/c.398delC |
| Pritchard et al, 2020 (A)United States | Case Report | CESD | Female | 120/120/n.r. | n.r. | HM | ET, HC,LH,HTG | KL,HS | LAL-D (n.r.)/ c.894 G > A / exon 4 |
| Pritchard et al, 2020 (B)United States | Case Report | CESD | Female | 120/120/n.r. | n.r. | HM, fever | ET, HC,LH,HTG | n.r. | n.r./c.57\_60delTGAG/ c.894G > A |
| Rabah et al, 2014 (Oman) | Case Report | Infantile | Male | 0.5/2/n.r. | Yes | HSM, AD, UH, Jcoarse facial features, HL | AC, A, ALF, HTG | HFC | 0,6%(b) / n.r. |
| Ries et al, 1996 (Mali) | Case Report | Infantile | Male | 2/3/n.r. | Yes | HSM, FTT | A, AC, | n.r. | <1% (c)c.903C>T/ c.903C>T |
| Riva et al , 2008 (Italy) | Case Report | CESD | Female | 60/60/n.r. | n.r | HM, PHTHepatocellular carcinoma | n.r. | MVS, C | LAL-D (c) / n.r. |
| Roytta et al, 1992 (Finland) | Case Report | Infantile | Female | 2/3/4 | Yes | HSM, AD | A | BMV | 4% (b) / n.r. |
| Sadhukhan et al, 2014 (England) | Case Report | Infantile | Male | 0/1/n.r. | No | HSM, D, V, FTT | BVL, ET, A | n.r. | 51%(B) / n.r. |
| Santillan-Hernandez, 2015 (A) (Mexico) | Case Report | CESD | Female | 2/108/n.r. | No | HSM, D, FTT, PHT | HTG, ET, EV | HS, MVS, PBF, C | <1% (b)c.253C>A /c.294C>G |
| Santillan-Hernandez, 2015 (B) (Mexico) | Case Report | CESD | Female | 6/48/n.r. | No | HM, FTT | HTG | Normal bone marrow | <1% (b)/c.253C>A /c.294C>G |
| Santos-Silva et al, 2018 (A) (Portugal) | Case Report | Infantile | Male | 2/4/n.r. | Yes | HSM, J, FTT, HL | A, AC, HTG, ET | HFC | 13,5% (b) <1% (c)c.966 + 2 T>G-intron 9 |
| Santos-Silva et al, 2018 (B) (Portugal) | Case Report | Infantile | Female | 4/5/n.r. | n.r. | HSM, AD UH, V, FTT, HL | A, AC, HTG, ET | HFC | 3,44%(b)c.509C>A/c.796G>T |
| Schaub J. et al, 1980 (Germany) | Case Report | Infantile | Female | 4/4/4 | n.r. | HSM, AD, D, V, FTT | A | BMVPBF | LAL-D (b) / n.r. |
| Shome DK et al, 2002 (Saudi Arabia) | Case Report | Infantile | Male | 0/2/4 | n.r. | HM, AD, D,V, ST, FTT | ET, A, HSi | Normal bone marrow | 5% (b) / n.r. |
| Silveira C. et al ,2007 (Spain) | Case Report | Infantile | Male | 60/84/n.r. | No | HSM, V | BVL, ET, AC | MVS, C | 0,3% (c) / n.r. |
| Sonmez et al, 2013 (Turkey) | Case Report | Infantile | Male | 1/4/4 | Yes | HSM, AD, FTT,Microcephaly | A, TR, ET, AC | BMV, HFC | 15,1% (b) / n.r. |
| Sreekantam S. et al, 2016 (England) | Case Report | CESD | Male | 60/84/n.r. | No | HSM, PHT | ET, HC, HTG | PBF, kV,C | 23% (b)c.894G>A / mutation on exon 6 |
| Stein et al, 2007 (Israel) | Case Report | Infantile | Female | 0/1/n.r. | Yes | Fetal ascites, HM, D, V ,NS,FTT | AC, BVL | n.r. | 0% (b) Doubly hetero-zygous for 2 mutations, G-5R and C60V |
| Surve et al, 2005 (India) | Case Report | Infantile | Male | 1/n.r/n.r. | No | HSM, AD, D, V, NS | A, AC | G, HLD, HS | 0% (c) / n.r. |
| Suzuki Y. et al, 1976 (Japan) | Case Report | Infantile | Male | 5/21/n.r. | No | HM, AD, D | A, BVL | BMV HS | LAL-D (b) / n.r. |
| Tadiboyina et al, 2005 (Canada) | Case Report | CESD | Male | 36/120/n.r. | No | HSM | HC, HTG | HLD, PBF | 7% (b)T insertion in exon 6/ c.894G>A |
| Tarantino et al, 1991 (A) (United States) | Case Report | CESD | Female | 6/40/n.r. | Yes | HSM | HC, HTG | PBF | 24% (c) / n.r. |
| Tarantino et al, 1991(B) (United States) | Case Report | CESD | Female | n.r./204/n.r. | Yes | HM | HC, HTG | Not performed | 4,3% (c) / n.r. |
| Taurisano et al, 2014 (Italy) | Case Report | Infantile | Female | 1/4/5 | No | HSM, AD, V, D, FTT, AS, HL | AC, ALF, ET, A , TR | BMV, HFC: HLD, kV | 18% (b) / n.r. |
| Tinsa F. et al, 2018 (Tunisia) | Case Report | Infantile | Female | 2/3/4 | Yes | HSM, AS, HL | AC, ET ,A | BMV | n.r./c.153C>A/ c.153C>A |
| Tommaso et al, 2018 (Brazil) | Case Report | CESD | Female | 24/n.r. /n.r. | n.r. | HM, AD | ET, HC, HTG | HLD, HS, MVS,kv, BRC | 2,5% (b) / n.r. |
| Tolar et al, 2009 (A) (United States) | Case Report | Infantile | Male | 1.5/2/5 | n.r. | FTT, ST | AC, HSi | HLD, MVS, kV, BRC | 6% (b) / n.r. |
| Tolar et al, 2009 (B) (United States) | Case Report | Infantile | Male | 12/17 /27 | n.r. | HM, D, ST | HSi | PBF | 3,8% (b) / n.r. |
| Tolar et al, 2009 (C) | Case Report | Infantile | Female | 1/1/n.r. | n.r. | HSM, D, ST | HSi | n.r. | 12,5% (b) / n.r. |
| Ťoukálková et al, 2017 (Czech Republic) | Case Report | CESD | Male | 84/156/n.r. | n.r. | IF | HC | HLD, MVS | 10% (b) / n.r. |
| Tylki-Szy-mańska1997 (A) (Poland) | Case Report | CESD | Male | 69/n.r. /n.r. | n.r. | HSM, AP | ET, HC | kV, C, BRC | 30,2% (b) / n.r. |
| Tylki-Szy-mańska1997 (B) (Poland) | Case Report | CESD | Female | 25/n.r. /n.r. | n.r. | HM | HC | PBF, kV, BRC | 25,6% (b) / n.r. |
| Tylki-Szy-mańska1997 (C) (Poland) | Case Report | CESD | Male | 67/n.r. /n.r. | n.r. | HSM | HC | BRC | 0,6% (b) / n.r. |
| Tylki-Szy-mańska1997 (D) (Poland) | Case Report | CESD | Male | 129/n.r. /n.r. | n.r. | HSM, AP | n.r. | n.r. | 25,6% (b) / n.r. |
| Tylki-Szy-mańska1997 (E) (Poland) | Case Report | CESD | Male | 156/n.r. /n.r. | n.r. | HSM | n.r. | PBF, kV, BRC | 10,9% (b) / n.r. |
| Tylki-Szy-mańska1997 (F) (Poland) | Case Report | CESD | Male | 25/n.r. /n.r. | n.r. | HSM | ET, HC | kV, C, BRC | 26,9% (b) / n.r. |
| Tylki-Szy-mańska1997 (G) (Poland) | Case Report | CESD | Female | 118/n.r. /n.r. | n.r. | HSM | HC | HS, MVS, kv | 14,2% (b) / n.r. |
| Valayanno-poulos et al, 2017 (A) (United States) | Case Report | CESD | Female | n.r./132/n.r. | n.r. | HSM | ET | PBF, MVS, kv | <0.05% (c)c.894G>A/ c.894G>A |
| Valayanno-poulos et al, 2017 (B) (United States) | Case Report | CESD | Male | 8 /108/n.r. | n.r. | HSM, ST | HC, HSi | n.r. | 32,3% (b) /c.894G>A/ c.894G>A |
| Valayanno-poulos et al, 2017 (C) (United States) | Case Report | Infantile | Male | 0 / n.r. /n.r. | n.r. | HSM, AD, D, V | AC, ET, HTG | HS, PBF | 7% (c) / Heterozygous mutations in exon 5 |
| Valayanno-poulos et al, 2017 (D) (United States) | Case Report | CESD | Male | 156/n.r. /n.r. | n.r. | IF, HM, | ET, HC, HTG | n.r. | 2,8% (b) / n.r. |
| Van Erum,1988(Belgium) | Case Report | CESD | Female | 24/ 48/n.r. | No | HM | ET, HC | n.r. | 0% (c) / n.r. |
| Wang TR, 1989 (Taiwan) | Case Report | Infantile | n.r. | 0 / 2/2 | No | HSM, AD, FTT | AC | BMV | 14,5% (b) / n.r. |
| Yanir et al, 2013(A)(Israel) | Case Report | Infantile | Male | 1 /n.r./72 | n.r. | HSM, D, V, FTT, ST, C | HSi, AC | n.r. | 10% (b) Missense mutation |
| Yanir et al, 2013(B)(Israel) | Case Report | Infantile | Male | 0.5 / 0.5/n.r. | n.r. | HSM | n.r. | n.r. | LAL-D (b) / n.r. |
| Zharkova et al, 2019 (Russia) | Case Report | CESD | Female | 204/216/n.r. | n.r. | HSM,Systemic Atherosclerosis | ET, HC, HTG, HSi | Liver: BRC, HS, KL, MVS | 0,25% (a) /c.894G>A/c.796G>T |

Abbreviations:

LAL-D, Lysosomal acid lipase deficiency; CESD, cholesteryl ester storage disease.

Clinical manifestations: HM, hepatomegaly; HSM, hepatosplenomegaly; SM splenomegaly; AI, adrenal insufficiency ; FTT, failure to thrive; AC, adrenal calcifications; AD, abdominal distension; AP, abdominal pain; AS, ascites; D, diarrhea; ST, steatorrhea; V vomits; J, jaundice; EV, esophageal varices; UH, umbilical hernia; IH inguinal hernia; IF : incidental finding intraoperative; PHT, portal hypertension; NS neurological symptoms; SH, systemic arterial hypertension; HL Hemophagocytic Lymphohistiocytosis

Laboratory findings: A, anemia; TR thrombocytopenia ; ALF, abnormal liver function; HC, high cholesterol; HTG, hypertriglyceridemia; LH, low HDL; ET, elevated transaminases.; BVL, peripheral blood showed vacuolated lymphocyte; DYS dyslipidemia. HSi hepatic steatosis in image studies.

Anatomic pathology tissue: DU, histiocytes vacuoles filled with lipidic material in lamina propria of duodenum; FC, foamy cells; BMV, bone marrow vacuolization, foamy macrophages; HFC hemophagocytosis; BRC, birefringent crystals/clefts; C, cirrhosis; F, fibrosis; G, intracytoplasmic glycogen; kV, Kupffer cell vacuolization; HLD, hepatocyte lipid deposition; HS, hepatic steatosis; MVS, microvesicular steatosis HV, hepatocyte vacuolization; KL, Kupffer cell lipid deposition; MBL, membrane bound lipid; MVS, microvesicular steatosis; PBF, portal-to-portal bridging fibrosis; PI, portal inflammation;

LAL activity of reference value (a) on dried blood spots, (b) on peripheral blood leukocytes, (c) on fibroblasts n.r., not reported.