The Phenotypic Spectrum of Dihydrolipoamide Dehydrogenase Deficiency in Saudi Arabia.

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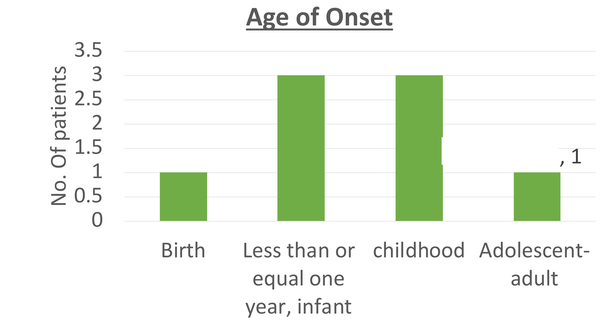
Introduction

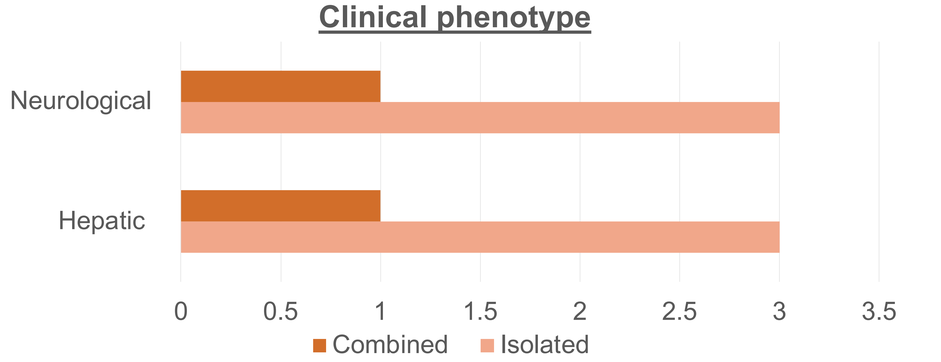
Dihydrolipoamide dehydrogenase deficiency (DLDD) is a rare metabolic disorder inherited in an autosomal recessive manner. DLDD is caused by a deficiency of the enzyme the dihydrolipoamide dehydrogenase, which is encoded by the DLD gene in 7q31.1. The complexity of this enzyme and the multiple biochemical functions would explain the variability (clinical heterogeneity) in affected patients, with a remarkable variability in phenotype, onset, and severity. There is no established genotype-phenotype correlation. The variability is directly related to the effects of the mutation on the activity of the enzymatic complex.

Material & Methods

We retrospectively reviewed the charts of pediatric patients from four major referral centers in Riyadh, Saudi Arabia, with a diagnosis of DLDD. Data were collected from collaborating physicians at the participating centers. inclusion criteria for the clinical review were confirmed homozygous pathogenic, likely pathogenic and variant of unknown significance in the DLD gene with a supportive clinical and biochemical phenotype.

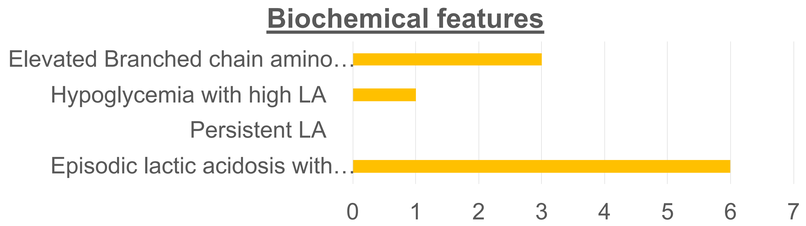
Results





Molecular test

DLD gene NM_000108:3	Patients
c.1436A > T, p.(Asp479Val)	2
c.623C > T, p.(Ser208Phe)	1
c.685G > T, p.(Gly229Cys)	5



Discussion & Conclusion

We describe the largest reported DLDD cohort in the Saudi population. The clinical and biochemical variability proved to be unpredictable on the sole basis of the genotypic characteristics or loss of enzymatic activity of the E3 Component. The most frequently detected variant in the sample was c.685G > T p. (Gly229Cys). To date, there is no effective treatment for this disorder, so early detection, molecular confirmation, and prenatal testing are needed to prevent severe disease such as DLDD.