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Genetic Testing for Hypertriglyceridaemia in the UK

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Background

Lipoprotein lipase deficiency (LPLD) is a rare disorder of lipid metabolism characterised by severe elevation of plasma triglycerides and circulating chylomicrons.[1-3]

Between 2013 and 2019, NHS Grampian hosted the only genetic testing service for suspected cases of the condition in the United Kingdom (UK).

Aims and Methods

We aimed to report the "real world" genetics data referred to the national centre for LPLD genetic testing and to provide a comprehensive overview to date of LPLD mutations from the UK.

Retrospective de-identified review of laboratory records for cases from the UK, referred to a single UK centre for LPLD testing (LPL, APOC2, GPIHBP1, APOA5 and LMF1) between November 2013 and June 2019.

Results

A total of 292 referrals requesting LPLD analysis were identified between November 2013 and June 2019.

- Of these, 181 (62%) were from cases domiciled in England, 99 patients (34%) were from Scotland and three (1%) were from Wales. The mean age at referral was 42 and most patients were male (62%).
- Primary referral reason [N=186] was confirmed hypertriglyceridaemia/hyperlipidaemia, followed by pancreatitis [N=66] and diabetes [N=21] (Fig. 1).
- The majority, in whom LPLD was confirmed, had homozygous (35.5%) or heterozygous (64.5%) variants in LPL (62/108), and homozygous (10.7%) or heterozygous (89.3%) variants in APOA5 (28/108) (Fig. 2).
- A further 28% of patients carried homozygous, heterozygous or compound heterozygous variants of unknown significance (VUS).

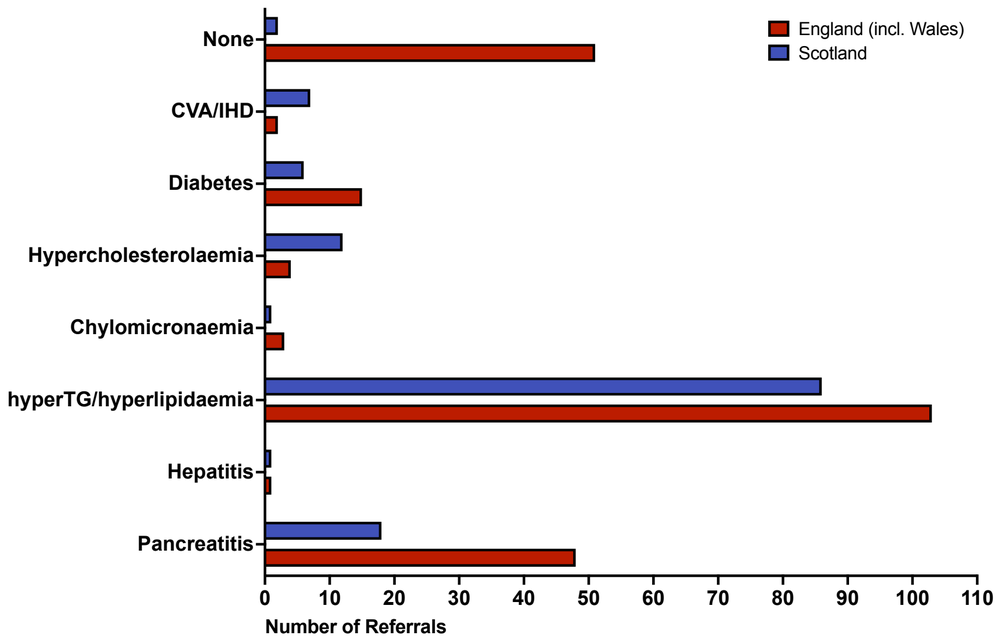

Fig 1. Presenting symptom as per referral location (England, Scotland, Wales).

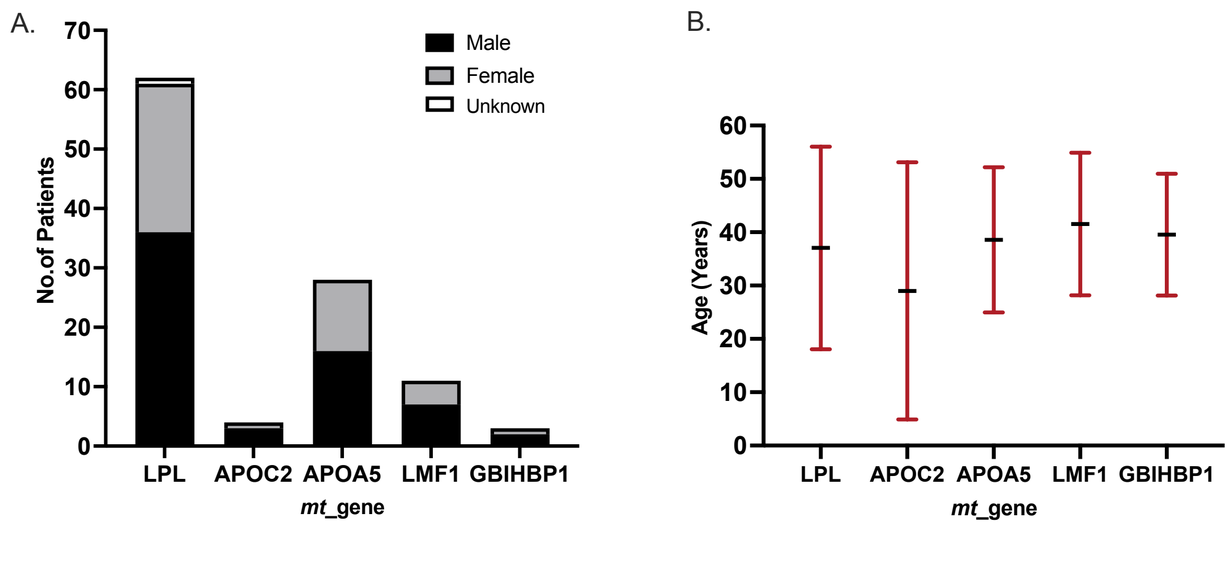

Fig 2. Gender (A) and age (B) distribution of positively diagnosed patients per mutant gene.

Conclusions

This is the first comprehensive review of LPLD mutations from the UK. In contrast to previously reported series, mutations in genes other than LPL were found to be common, reflecting the outbred nature of the UK population, and highlighting the utility of genetic diagnosis in LPLD.

References

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