

Diagnostic utility of the multigene panel in GSDs: update of a Brazilian cohort

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INTRODUCTION

Hepatic glycogen storage diseases (GSD) are a group of rare genetic disorders in which glycogen cannot be metabolized to glucose in the liver because of enzyme deficiencies along the glycogenolytic pathway. GSDs are recognized diseases that can occur without the full spectrum, and with overlapping in symptoms. The objective is to present an update the of the Brazilian Hepatic GSD cohort genomically investigated by our group.

OBJETIVES

To present an update the of the Brazilian Hepatic GSD cohort genomically investigated by our group.

METHODS

One hundred and forty-five GSD patients (n=145) were included (125 have been previously reported). Patients had clinical diagnosis of GSD and were analyzed by a multigene panel in Ion Torrent platform (figure 1).

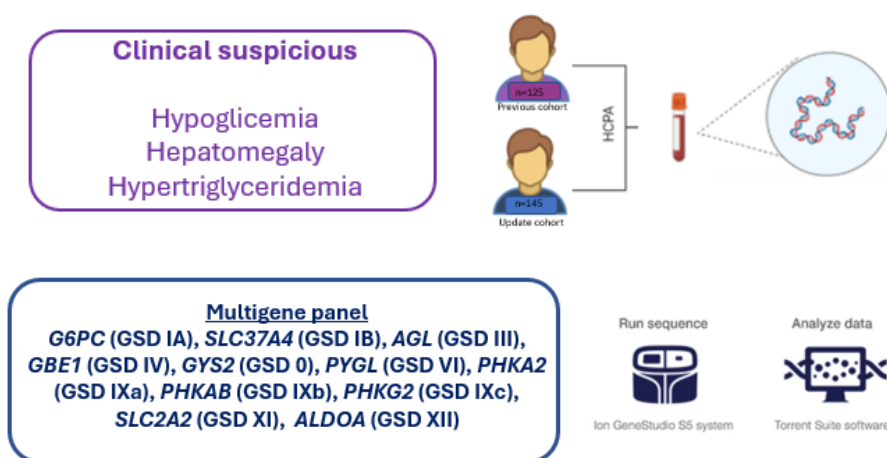


Figure 1: Analysis workflow

RESULTS AND DISCUSSION

In the update cohort (n= 20 patients), 15 variants were identified. The most frequent GSD was type Ia (n=10), followed by Ib (n=8), GSDIXa (n=1) and GSDIXb (n=1). Considering the complete cohort, the most frequent GSD was Ia (n=63/145), followed by Ib (n=31/145; fig. 2) . The most frequent variants were p.Arg83Cys (n=48/250) and p.Gln347* (19/250) in G6PC gene, and p.Leu348Valfs (27/250) in SLC37A4 gene (fig. 3).

GSD types in total cohort

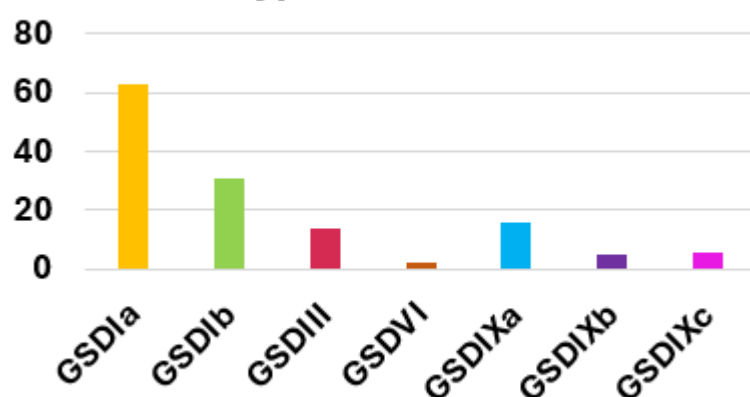


Figure 2: GSD types identified in 20 patients of total cohort

Most frequent variants

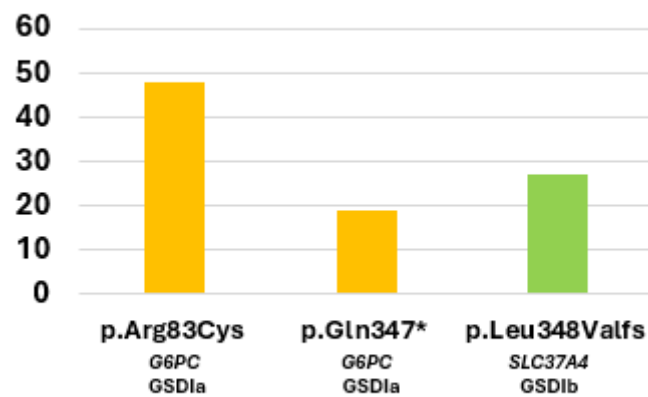


Figure 3: Most frequent variants in 250 alleles.

CONCLUSION

The study presents the updated cohort of Brazilian patients with hepatic GSDs and validate the previous results presenting data from the world's largest cohort of GSDs. The GSDs as a group involves 11 different genes with wide allelic heterogeneity. We determined the clinical utility of multigene panels through diagnosis of all patients enrolled in the update study (20/20) and in a widely variable cohort. The most common variants in our cohort are also the most frequent in other countries. Molecular diagnosis of hepatic GSDs is a great step in the characterization of different forms of these diseases with similar clinical symptoms, avoiding hepatic biopsy and speeding results.