Next generation sequencing results in 142 patients with congenital hyperinsulinism

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OBJECTIVES

Congenital hyperinsulinism (HI) is a life-threatening disorder characterized by hypoglycemia due to dysregulated secretion of insulin from pancreatic β-cells. Genetic diagnosis is essential for patient management. NGS technologies are relatively new method which gives the ability to generate large amounts of sequence data in a relatively short period of time enabling timely diagnosis.

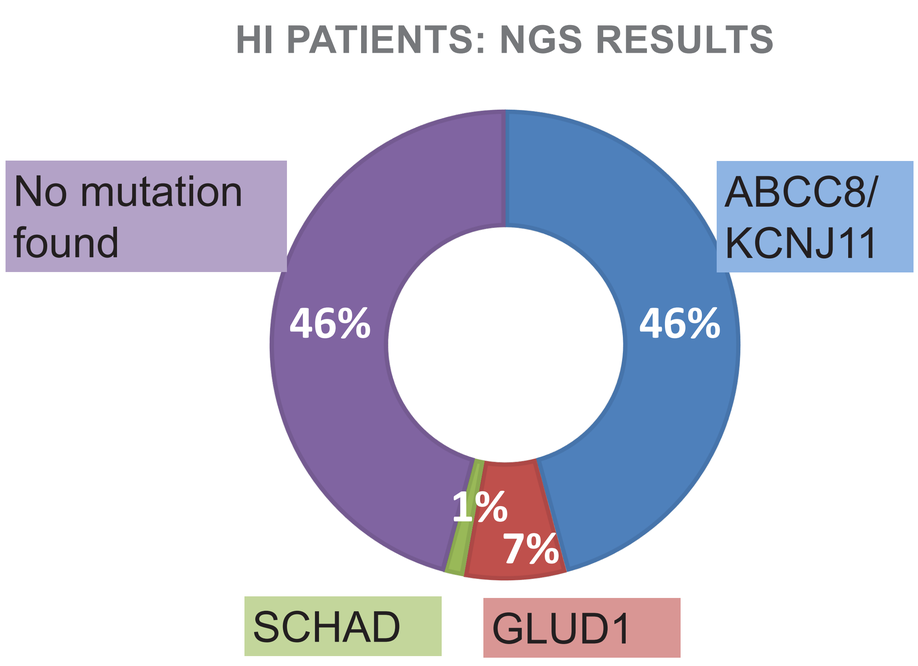
METHODS

We performed NGS in 142 patients (66 males, 76 females) with HI and evaluated the results.
The diagnosis of HI was based on clinical presentation and confirmed biochemically by the presence of detectable serum insulin during hypoglycemia.

NGS (Ion Torrent platform): *GCG, GLUD1, WFS1, HNF1A, GCK, INS, HNF1B, ABCC8, HNF4A, RFX6, PTF1A, NEUROD1, AKT2, ZFP57, INSR, EIF2AK3, PPARG, PAX4, PDX1, GLIS3, KCNJ11, SLC16A1, FOXP3, BLK, CEL, KLF11, SCHAD, GCGR.*

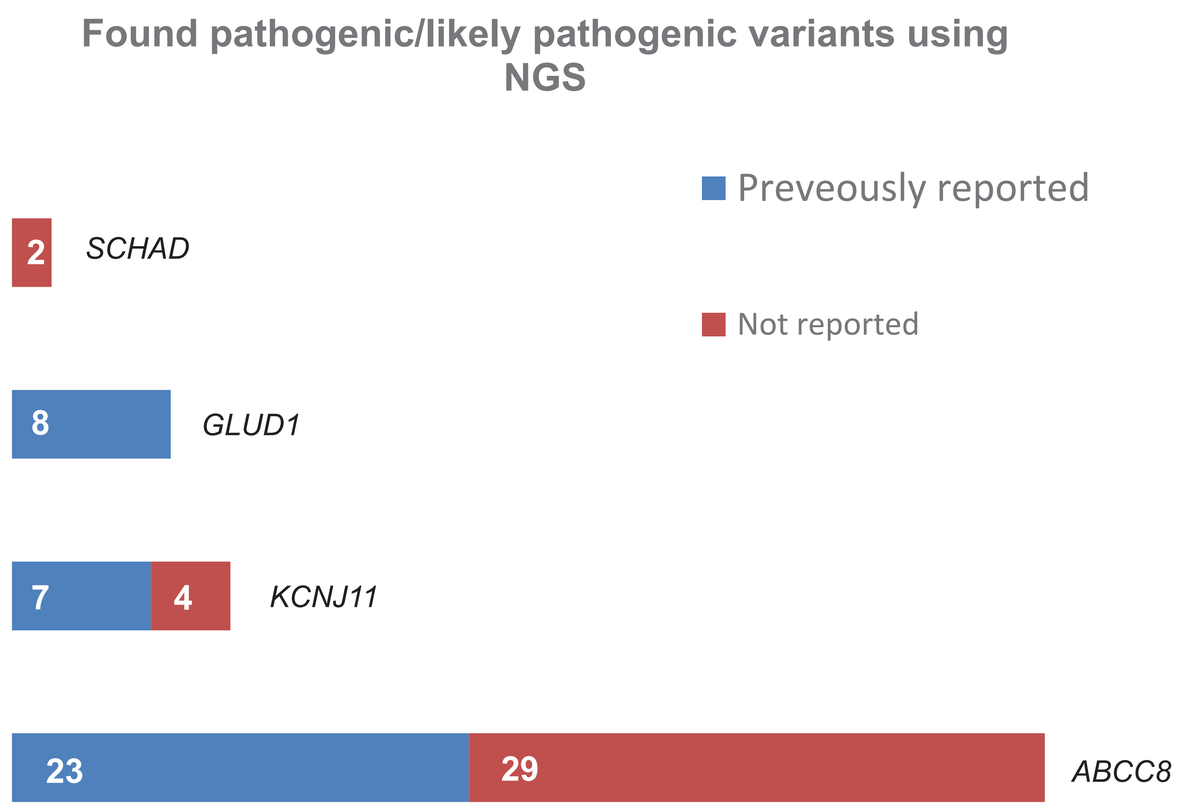
RESULTS

In summary 77 patients (54.2 %) were found to carry pathogenic/likely pathogenic variants in the HI related genes.



A total of 73 different pathogenic/likely pathogenic variants in 77 patients were found:

- 52 *ABCC8* variants (reported 23/52)
- 11 *KCNJ11* variants (previously reported 7/11)
- 8 variants related to *GLUD1* (previously reported 8/8)
- 2 heterozygous variants in *SCHAD* (not reported formerly)



Some frequent pathogenic/likely pathogenic variants were found in several patients:

- a combination of monoallelic c.G1096A:p.G366R in *KCNJ11* and c.C1038G:p.Y344X in *ABCC8* (4 children)
- *ABCC8* heterozygous c.G1332T:p.Q444H (3 patients)
- *ABCC8* heterozygous c.G4516A:p.E1506K (3 patients)

CONCLUSIONS

The genetic cause of HI was found in 54% of the patients with the use of NGS technologies. These data are comparable to results of Sanger sequencing. According to our experience, NGS technologies proved to be comparatively fast and trustworthy method.

Conflict of interests

Authors declair no conflicts of interests.