BACKGROUND

- Mutations of POU1F1 have autosomal recessive inheritance, and phenotypically present with small or normal anterior pituitary gland, with normal posterior pituitary and infundibulum without extra pituitary signs.
- Patients present with Growth Hormone (GH) and Prolactin (PRL) deficiency with variable presentations of TSH deficiency.
- Children with CO-GHD secondary to genetic mutation are more likely to have persistent GHD in adulthood.

OBJECTIVES

- To describe the clinical course and outcome at of two siblings diagnosed with compound heterozygous novel mutations of the POU1F1 gene.
- Both cases have isolated GHD with normal pituitary structure in exon 3 and 4 - p.K166E and P.E224K respectively.

CASE HISTORY

- **Case 1**: Presented with severe growth failure, short stature (SS) and complete isolated GHD at the age of 4 years .
- Low IGF 1 SDS and absence of GH peak on GH stimulation test.
- He had an excellent response to GH treatment.
- At the final height (50th centile), GH status re-evaluation by insulin tolerance test (ITT) revealed persistent severe GHD deficiency.

- **Case 2**: The younger sister presented in the neonatal period with severe hypoglycaemia.
- Diagnosis was confirmed with low IGF 1 SDS, low GH level in neonatal period, clinical growth failure at the age of 2 months and a failed glucagon stimulation test. She has responded well to GH treatment (now 25th centile).

CONCLUSIONS

- Severe GHD and very early presentation are the main pointers to genetic /pathological causes of CO-GHD even in presence of normal pituitary structure.
- This heterozygous mutation in exon 3 and 4 of the POU1F1 gene in this sibling pair is novel.
- The persistence of GHD after attainment of final height in case 1 emphasised the importance of identifying the underlying pathology of CO-GHD. This has facilitated the transition process in this patient and his preparation of the young adults for future possible outcomes.
- A GH level in the neonatal period associated with hypoglycaemia is a useful diagnostic tool of neonatal GHD especially in challenging cases where GHD is isolated and pituitary structure on imaging is normal.

REFERENCES