

INTRODUCTION

Hypogonadotrophic hypogonadism (HH) is a rare condition caused by gonadotrophin deficiency, where a definitive diagnosis is often hard to reach

AIM

clinical, describe biochemical and genetic findings in cases with suspected HH in the West of Scotland who were referred for genetic analysis between 2016 and 2020

METHOD

Information was collected on clinical assessment including presenting symptoms, family history, gonadal extra-gonadal features, and biochemical and molecular genetic analysis using a panel of 21 HH genes (ANOS1, CHD7, CUL4B, FEZF1, FGF8, FGFR1, FSHB, GNRH1, GNRHR, KISS1R, LHB, NR0B1, PROK2, PROK2R, SEMA3E, SOX10, SOX2, SPRY4, TAC3, TACR3, WDR11)

REACHING A DEFINITIVE DIAGNOSIS OF HYPOGONADOTROPHIC HYPOGONADISM – EXPERIENCE OF A MULTIDISCIPLINARY DIAGNOSTIC SERVICE

Supitcha Patjamontri¹, Malika Alimussina¹, Louise A Diver², Martin McMillan¹, Jane D McNeilly³, Angela K Lucas-Herald¹, Marie Freel⁴, Greg Jones⁵, Andrew Kernohan⁴, Robert Lindsay⁴, Neil McGowan⁶, Colin Perry⁴, Aparna Sastry⁷, M Guftar Shaikh¹, Edward S Tobias^{2,8}, Ruth McGowan^{1,2}, S Faisal Ahmed¹

1. Developmental Endocrinology Research Group, University of Glasgow, Royal Hospital for Children, Glasgow, UK., 2. West of Scotland Clinical Genetics Service, Queen Elizabeth University Hospital, Glasgow, UK.3. Biochemistry Department, Queen Elizabeth University Hospital, Glasgow, UK. 4. Department of Endocrinology, Queen Elizabeth University Hospital, Glasgow, UK 5. Department of Endocrinology, Gartnavel General Hospital, Glasgow, UK 6. Department of Endocrinology, Royal Alexandra Hospital, Paisley, UK 7. Assisted Conception Service, Glasgow Royal Infirmary, Glasgow, UK 8. Academic Medical Genetics and Pathology, University of Glasgow, Queen Elizabeth University Hospital, Glasgow, UK.





RESULTS

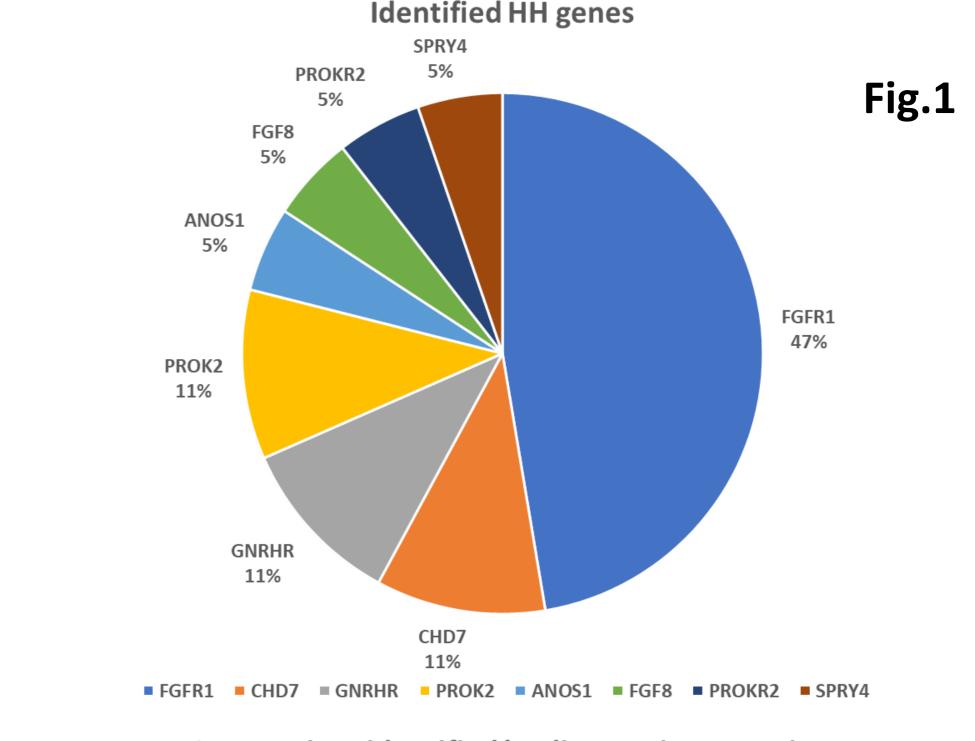
Between 2016 to 2020, thirty cases with suspected HH (19 male, 11 female) and a median age of 18.3 yrs (range, 1.8, 48.3) had genetic analysis as part of routine clinical investigations

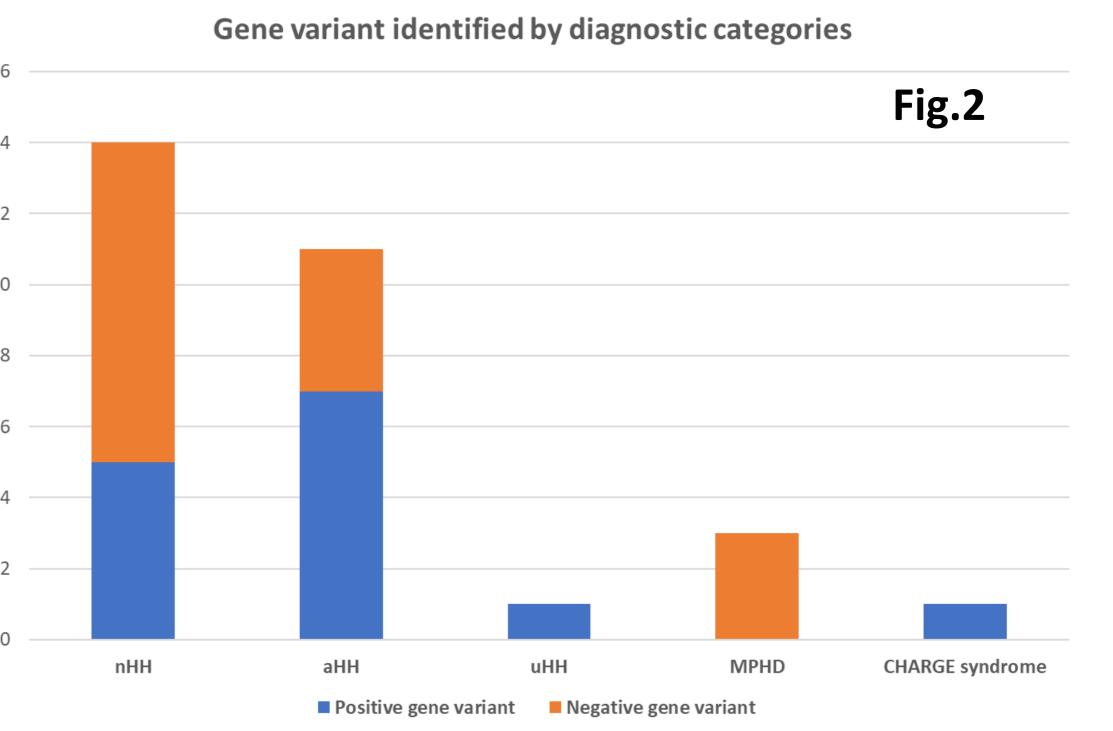
These patients included:-

- 11 (37%) with anosmic HH (aHH)
- 14 (47%) with normosmic HH (nHH),
- 1 (3%) with uncertain sense of smell (uHH)
- 3 (10%) with multiple pituitary hormone deficiency (MPHD)
- 1 (3%) with CHARGE syndrome

Major Findings:-

- A positive family history related to HH was present in 9/30 patients (30%)
- Delayed puberty was the commonest presenting symptom, found in 12/30 patients (40%)
- Apart from anosmia in the 11 patients with aHH, 6/30 (20%) had other extra-gonadal features
- Olfactory neuroimaging was abnormal in 5/22patients (23%) who had MRI studies
- 19 gene variants of ACMG class 3-5 were identified in 8 genes in 14/30 (47%) (Figure 1)
- Although likelihood of a gene variant was greater in those with anosmic HH, there were several cases of nHH who also had a gene variant identified (Figure 2)





CONCLUSIONS

- Almost 50% of patients with HH undergone had targeted who genetic analysis had a variant identified
- A low threshold is required to suspect a diagnosis of HH even if classic features of HH do not exist

REFERENCES

- 1. Young J, Xu C, Papadakis GE, et al. Clinical Management of Congenital Hypogonadotropic Hypogonadism. Endocr Rev. 2019;40(2):669-710.
- 2. Cangiano B, Swee DS, Quinton R, Bonomi M. Genetics congenital hypogonadotropic of hypogonadism: peculiarities and phenotype of disease. Genet. oligogenic Hum 2021;140(1):77-111.

ACKNOWLEDGEMENTS

We would like to thank all members of the Glasgow DSD team for their help and support

Funded by The Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok Thailand

CONTACT INFORMATION

Supitcha Patjamontri, M.D. Developmental **Endocrinology Research Group, University of** Glasgow, Royal Hospital for Children, Glasgow,

supitcha.pajmontri@glasgow.ac.uk

