

2. Executive summary of the project

Genetic studies on growth hormone deficiency (GHD) leading to short stature have not been carried out previously in Sri Lanka. We investigated a cohort of patients clinically and biochemically confirmed to have GHD. Mutations and sequence variants of the *GHI* gene coding for growth hormone (PCR and sequencing) and *GHRH-R* gene coding for the GH releasing hormone receptor (PCR and sequencing or PCR/SSCP and sequencing), and gross deletions of the *GHI* gene (PCR/RFLP) were analysed. Novel mutations observed were subjected to bioinformatic analyses to discern pathogenicity. *GHRH-R* codon 72 mutation was found in 8 patients from 6 families following screening of 95 patients. *GHI* gene was sequenced in 48 patients negative for this mutation. Three pathogenic mutations of the *GHI* gene (2 previously reported and one novel) and several other sequence variants were observed. Promoter region of *GHI* gene showed the presence of variants reported to be associated with altered expression of *GHI* gene. But these variants were also seen among the healthy controls of normal height. Only one patient carried the 7 kb deletion of *GHI* gene. Apart from the codon 72 mutation considered to be prevalent in the Indian subcontinent, *GHRH-R* gene showed several other variants but only one novel mutation appeared to be pathogenic. When only the patients with complete isolated growth hormone deficiency in the study group is considered 12 patients out of 34 had either *GHI* or *GHRH-R* abnormalities giving a combined prevalence of 35.2 % for pathological or possibly pathological mutations among them.

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