Association between thyroid specific genotypic variation and phenotypic expression of dyshormonogenetic goiter and Hashimoto's thyroiditis in children and adolescents

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OBJECTIVES

Background: Though very common, thyroid specific genetic studies on hypothyroidism in children is lacking from South India

In children and adolescents - with hypothyroidism due to dyshormonogenetic goiter (DH) and Hashimoto's thyroiditis (HT)

- To screen for NIS, DUOX2 and TPO gene mutations
- To correlate between mutations and hypothyroid phenotype

METHODS

- Genomic DNA was extracted from peripheral blood leucocytes
- PCR and direct sequencing were used to analyse for NIS, DUOX2 and TPO genes
- Detailed clinical, biochemical and follow-up data were recorded in a structured proforma
- Subjects with hypothyroidism were treated with thyroxine replacement
- Detailed genetic analysis with 142 SNP (single nucleotide peptides) and 8 sets of primers were done.

RESULTS

- Age of the cohort was 11 ± 4.5 (5 – 17) years
- F: M ratio was 17:3
- Hypothyroidism was overt and subclinical in 14 and 6 patients respectively
- Family history of hypothyroidism was present in 7 patients (35%)
- Genetic analysis shows that heterozygous NIS mutations were seen in 5 children with HT and in 3 children with DH
- A homozygous mutation was picked up in a child with HT
- Heterozygous TPO mutations found in 2 cases of HT
- No mutation was found in DUOX gene

Sequence ID: lcl|4/183 Length: 298 Number of Matches: 1

Range 1: 30 to 298 Graphics Next Match Pr

Score	Expect	Identities	Gaps	Strand
375 bits(203)	6e-109	250/269(93%)	17/269(6%)	Plus/Plus

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Query  1    GTGCTTGGCGTGC-GTCGGA-G-CTATCGCT-TGGCCTC-AGTTCCTCTGG-TGTGCCTG  54
            ||||| |||||||| ||||||  | |||||||| |||||||| |||||||||| |||||||||
Sbjct  30   GTGCTGGGCGTGCCGTCGGAGGCCTATCGCTATGGCCTCAAGTTCCTCTGGATGTGCCTG  89

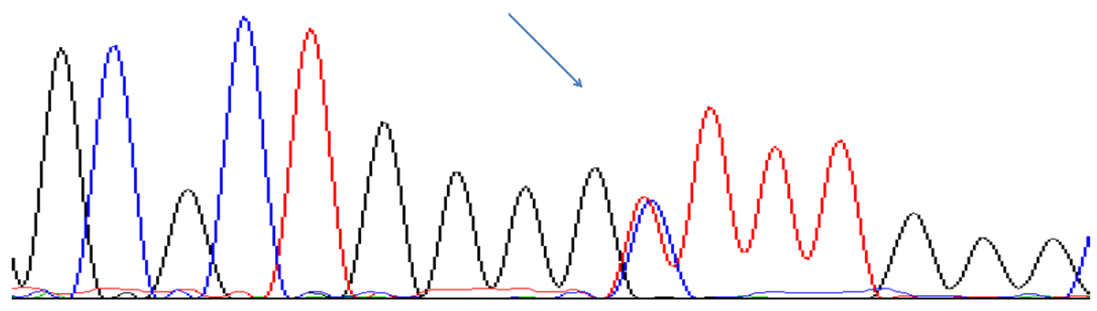
Query  55   GGCCAGCTTCTGAACTCGGTCCTCACCGCCCTGCTCTTCA-GCCCGTCTTCTACCGCC-G  112
            |||||||||||||||||||||||||||||||||||||||| |||||||||||||||||| |
Sbjct  90   GGCCAGCTTCTGAACTCGGTCCTCACCGCCCTGCTCTTCATGCCCGTCTTCTACCGCCTG  149

Query  113  GGCCTCACCAGCACCTAC-AGGTACCGGACAGAGGCCCGGGGGTAGGACCTGCCCCACTG  171
            |||||||||||||||||| ||||||||||||||||||||||||||||||||||||||||||
Sbjct  150  GGCCTCACCAGCACCTACGAGGTACCGGACAGAGGCCCGGGGGTAGGACCTGCCCCACTG  209

Query  172  GC-GTGCTGGGACCCCGTGTGGGGGAGGCGCTGGGGTTTTGGGCCGCT-TAC-GGAG-AC  227
            || |||||||||||||||||||||||||||||| |||||||||| ||| |||| ||
Sbjct  210  GCAGTGCTGGGACCCCGTGTGGGGGAGGCGCTGGGGCTTTGGGCCGCTGTACAGGAGGAC  269

Query  228  -CG-ATGGCACCTCG-T-CTTTAACGGAA  252
             || |||||||||| | ||||||||||
Sbjct  270  GCGGATGGCACCTCGGTGCTTTAACGGAA  298
```

A variation from C>T(homozygous mutation) was found at 17983561 position(rs:740695).(06)(HT)



CONCLUSIONS

- NIS gene mutations appears to be most prevalent mutations in HT and DH amongst South Indian children in this study

•The iodine deficiency and ethnic factors may be responsible for this pattern. Further studies are needed to characterize hypothyroid phenotypes in children.

(**Key words:** Dyshormonogenetic goiter, Hashimoto's thyroiditis, NIS mutation, Genotype, Phenotype)

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