CLINICAL AND MOLECULAR PRESENTATION OF CONGENITAL HYPOTHYROIDISM CAUSED BY THYROGLOBULIN GENE MUTATIONS

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INTRODUCTION

Congenital hypothyroidism (CH) characterized by a deficient secretion of thyroid hormone in newborn (1). It is the most common endocrine disease in the children with an incidence rate about 1:3000 live births in Saudi Arabia (2). Thyroid dysgenesis and dyshormonogenesis are the most common causes of CH. Thyroid dyshormonogensis commonly inherited as autosomal recessive disorders (3). Although Thyroglobulin followed by TSHR mutations are the most common genetic defects in Saudi patients (4), there was no enough data regarding their clinical manifestations and management of these cases.

AIM

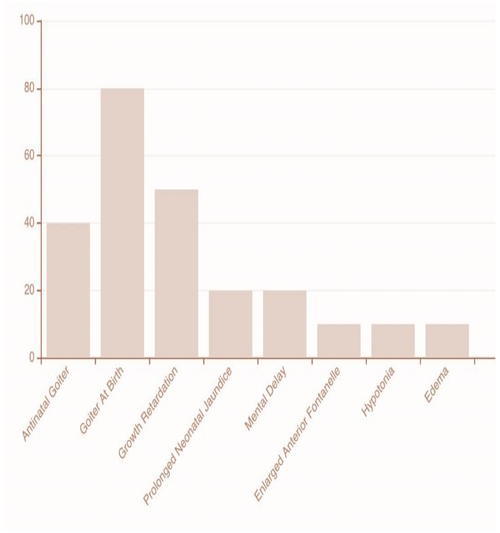
1. To describe the clinical, biochemical and molecular features of patients with congenital hypothyroidism related to thyroglobulin defects.
2. To highlight the genetic variant of mutations that caused thyroglobulin defects
3. To describe their response to management

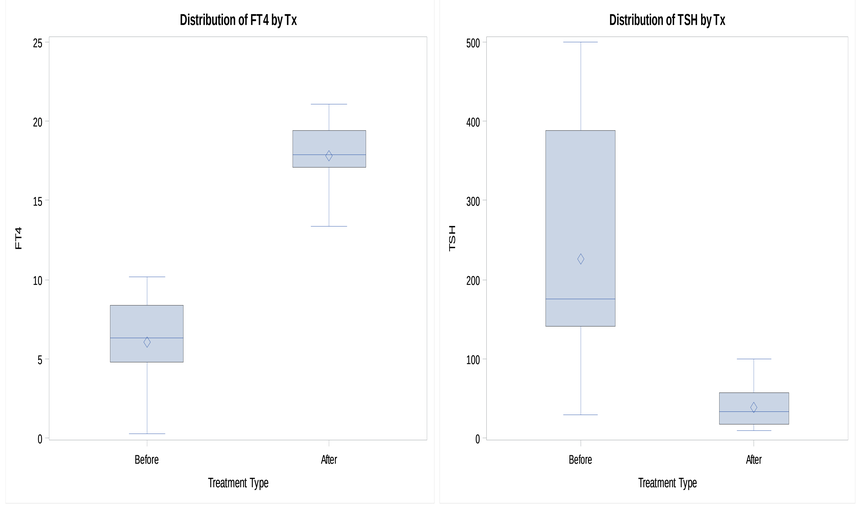
METHOD

A retrospective cohort study, conducted at King Faisal Specialist Hospital and Research Centre, Riyadh, Saudi Arabia. Including 10 patients who genetically confirmed to have CH secondary to Thyroglobulin gene mutation. Medical Charts were reviewed for clinical, biochemical and radiological data.

RESULTS

8/10 (80%) had strong family hx of congenital hypothyroidism. 4/10 patients (40%) presented with goiter antenatally and received multiple intra-uterine Thyroxin injection, 8/10 (80%) presented with enlarged goiter and 5/10 (50%) with growth retardation. Those patients required large dose of Thyroxin (mean dose of 20 mcg/kg/week). Biochemically, all patients presented with high TSH and low fT4. Interestingly, all patients have persistently high TSH level even with upper-normal level of fT4 (P=0.0022). We found 3 previously reported homozygous mutation in TG gene, and one compound heterozygous new mutation.





TSH and fT4 levels before and after treatment. patients have persistently high TSH level even with upper-normal level of fT4 (P=0.0022).

CONCLUSIONS

This study is the largest cohort series to date describing the clinical and molecular features of CH secondary to Thyroglobulin gene mutation worldwide, as well as their management and prognostic indicators. Anti-natal treatment with fetal thyroxine was effective in reducing the size of the goiter, preventing the need of thyroidectomy and lower the required treatment dose. It will contribute significantly to the understanding of genetic mutations underlying the congenital hypothyroidism related to thyroglobulin mutation in Saudi population.

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