Genetic Studies in Congenital Hypothyroidism; A Regional Study

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Background: Congenital hypothyroidism (CH) is considered as the most common endocrine disorder in neonates. CH may be caused by defects in the thyroid gland (dysgenesis) or in one of the stages in the synthesis of thyroid hormones (dyshormonogenesis).Early diagnosis and treatment of neonates with CH is crucial for their neurological development and preventing its related mental retardation.

CH screening program have made the opportunity to achieve the mentioned goals. CH screening program in Isfahan-Iran was initiated in 2002 and continued until 2005 when it integrated with the nationwide CH screening.

Results of CH screening indicated that prevalence of CH is high in Isfahan. Moreover the etiologic feature of CH with higher rate of dyshormonogenesis was not similar to that reported by other studies worldwide. To determine the causes of mentioned differences as well as pathophysiology of CH many genetic studies was performed in Isfahan. In this review the findings of the genetic studies are presented.

The role of Thyroid transcription factor 1 (TTF1) and TTf2, TSH receptor (TSHR) and paired box transcription factor 8 (PAX8) genes studied among CH patients with dysgenesis. We found a known polymorphism in ser 273 of TTF2 gene in 74% unrelated patients and a heterogen polymorphism for TSHR gene.

In dyshormonogenetic CH patients, thyroid peroxidase (TPO), two mutations (T354P and G395R) of Sodium/Iodide Symporter (*NIS*) and four mutations (R434X, Q36H, R376W, and D506N) of Dual Oxidase 2(DUOX2) were studied. One homozygous missense mutation at exon 15 in one patient and seven different single nucleotide polymorphisms in exons 1, 7, 8, 11, and 15 of TPO gene were detected.

Conclusion: Though some mutations in both dysgenetic and dyshornrmonogenetic CH patients were detected but it seems that screening of the whole length of the involved genes can be helpful to determine the cause of CH in our patients