ORIGINAL RESEARCH PAPER
Volume-9 | Issue-1 | January-2020 | PRINT ISSN No. 2277 - 8179 | DOI : 10.36106/ijsr
INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

MUTATIONAL STUDY OF HYPOTHYROIDISM AND HYPERLIPIDEMIA LIPID METABOLISM REGULATES VIA THYROID HORMONE RECEPTOR BETA GENE

Biochemistry

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ABSTRACT

Thyroid dysfunction has a great impact on lipids.Hypothyroidism is relatively common and is associated with an unfavorably affect on lipids. Hypothyroidism is present in 1.5% to 15% of the patients with hyperlipidemia.The mostcommon cause of resistance to thyroid hormone (RTH) is Heterozygous thyroid hormone receptor Beta (THRB) Gene Mutation. Thyroid hormone plays an important role in Thermogenesis and Maintenance of Homeostasis. The present study reviews the evidence that lipid metabolism regulates via thyroid hormone receptor. The liver is an important target organ of thyroid hormone. However hepatic target genes have been identified and known about the pattern of their regulation by thyroid hormone.

KEYWORDS

Gene Mutations, Hypothyroidism, Hyperlipidemia

INTRODUCTION

Thyroid dyshormonogenesis results from mutation is one of several genes involved in the production of thyroid hormones. These genes include DUOX2 DUOXA2, DUOX1, TPO,TG,SLC26A4,SLCRA5 mutations in each of these genes disrupt a in thyroid hormone synthesis, leading to abnormally low levels of these hormones. Mutations in the APOB, LDL, LDARAP1 and PCSK9 genes cause hyperlipidemia. These genes were selected to be sequenced in this study. All exons and exon – introns boundaries of these were amplified by multiplex PCR using the 48 x 48 Accus Arraay microfluid platform (fluid digm) according to the manufacturer's protocol. Primers were designed by iPLEX Assay Designed software (Sequences). Deep sequencing of these amp icon libraries was carried out by using the Hiseq2500 or Hiseq3000 platform. To avoid base pair variants caused by multiplex PCR, target sequence were amplified and deeply sequenced in duplicate for each sample.

MATERIALS AND METHODS

A total number of 300 patients (n=300) and 200 controls (n=200) of age group 40 - 60 years of either sex were taken for the study. The patients were on the medication of hypothyroidism and hyperlipidemia. Their lipid profiles were estimated on Cobas fully automated clinical chemistry analyzer and hormonal parameters were measured on Mini Vidas especially Thyroid Stimulation Hormone (TSH) were carried in Department of Biochemistry, Bhaskar Medical College and General Hospital, R.R District, Telangana State, India.Their Gene Mutations and Point Mutations were carried on Biorad PCR Machine at Biochemistry Laboratory, Owaisi Hospital & Research Centre (a teaching hospital to Deccan College of Medical Sciences, Hyderabad, Telangana State India)

RESULTS

Table 1

Biochemical Parameters of Hyperlipidemia

Parameters	Patients (n=300)	Controls (200)	p value
Total Cholesterol (mg/dl)	364	158	0.001
HDL Cholesterol (mg/dl)	85	44	0.001
LDL Cholesterol (mg/dl)	178	77	0.001
Triglycerides (mg/dl)	318	114	0.001
VLDL Cholesterol (mg/dl)	64	22	0.001

The Biochemical Parameters were compared with mean S_+D p value is common

Table 2

Biochemical Parameters of Hypothyroid

Parameters	Patients (n=300)	Controls (200)	p value
TSH(mU/L)	160	0.3 – 4.7	0.01
T3 (nmol/L)	0.8	0.92 – 2.78	0.01
FT3(pmol/L)	0.11	0.22 – 6.78	0.01
T4(nmol/L)	42	58 – 140	0.01
Ft4 (pmolL)	5.2	10.33	0.01

The Biochemical Parameters were compared with mean S_+D p value

MUTATIONAL STUDY

These genes include DUOX2 DUOXA2, DUOX1, TPO,TG,SLC26A4,SLCRA5 mutations in each of these genes disrupt a in thyroid hormone synthesis, leading to abnormally low levels of these hormones. Mutations in the APOB, LDL, LDARAP1 and PCSK9 genes cause hyperlipidemia. These genes were selected to be sequenced in this study. All exons and exon – introns boundaries of these were amplified by multiplex PCR using the 48 x 48 Accus Arraay microfluid platform (fluid digm) according to the manufacturer's protocol. Primers were designed by iPLEX Assay Designed software (Sequences). Deep sequencing of these amp icon libraries was carried out by using the Hiseq2500 or Hiseq3000 platform. To avoid base pair variants caused by multiplex PCR, target sequence were amplified and deeply sequenced in duplicate for each sample. The results were found positive for mutations.

CONCLUSION

With reference to table 1 the values of lipid profiles of the patients were found high compared to controls. The high values indicate the presence of hyperlipidemia. Where as in table 2 Thyroid Stimulating Hormone (TSH) value is found very much high and other hormones were found lesser the normal values which indicate the presence of hypothyroidism. With reference to mutational study genes disrupt a in thyroid hormone synthesis , leading to abnormally low levels of these hormones cause hyperlipidemia.

DISCUSSION

Clinical observations showing inverse correlation between the degree of hypelipidemia and thyroid status coupled with the fact that *APOA5* is a major determinant of lipid homeostasis prompted to explore the potential regulation of this recently identified gene by TH.

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