PREFACE

The recent research revealed that thyroid abnormality is the source of many other organ disorders (Dimitriadis et al., 1991, Hoppner and Seitz, 1989). But it is not very much clear how thyroid dysfunction modulates the function of other organs in the body. Therefore, further investigation needed to unveil the detailed sequential events of cellular and biochemical changes in rat upon thyroid dysfunction and their relationship with the clinically defined thyroid patients in our population.

Thyroid hormone biosynthesis is mediated by a key enzyme thyroid peroxidase (TPO). TPO is a rate limiting enzyme of thyroid hormone biosynthesis and is required for the coupling of iodine to tyrosine molecule to form thyroid hormones. Methimazole, an inhibitor of TPO enzyme was used to induce hypothyroid and thyroxine to induce hyperthyroid conditions in experimental rat. The investigation includes the parameters like T3 and T4 hormones, liver glycogen, SGPT, SGOT, OGTT (Oral Glucose Tolerance Test), histology of pancreas, liver and testis.

The thyroid hormone level may change upon the mutations/ polymorphism of TPO gene. Mutations in the thyroid peroxidase (TPO) gene (particularly non-synonymous Single Nucleotide Polymorphisms in coding regions) can lead to severe defects in thyroid hormone production, due to total iodide
Thyroid dysfunction states with special reference to polymorphism of thyroid peroxidase (TPO) gene

organification defects (TIOD) or partial iodide organification defects (PIOD). Therefore, the investigation was also aimed to understand whether hypothyroid patients are associated with mutations/polymorphism (s) in TPO gene coding sequence.

The results showed significant changes in T₃, T₄ hormones, liver glycogen, serum SGPT and SGOT in both hypothyroid and hyperthyroid rat. Significant alterations of OGTT curves observed in both hypothyroid and hyperthyroid groups of rat.

Tissue samples from liver, pancreas and testes exhibited significant changes in cytomorphology upon experimental induction. Sequence analysis of the selected exons in TPO gene demonstrated a number of mutations in patient samples when compared with the normal individuals. The patients showing mutations in TPO gene corroborates the clinical manifestations. Therefore, our results clearly indicate the mutations in TPO gene may be associated with hypothyroidism.