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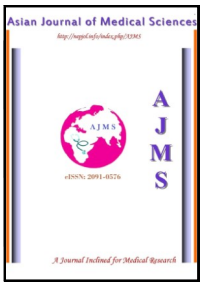

Mutation Analysis of the LDL Receptor Gene in Indian Families with Familial Hypercholesterolemia

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Abstract

Objective: Familial Hypercholesterolemia (FH) is a metabolic disorder inherited as an autosomal dominant trait characterized by an increased plasma low-density lipoprotein (LDL) level. The disease is caused by several different mutations in the LDL receptor (LDLR) gene. Several mutations have been reported in this gene in patients from several ethnic groups. Early identification of individuals carrying the defective gene could be useful in reducing the risk of atherosclerosis and myocardial infraction by the available therapeutic methods. The techniques available for determining the number of the functional LDLR molecules are difficult to carry out and expensive. Our study presents mutation analysis of the LDLR gene in 24 Indian families with FH.

Material & Methods: *Peripheral blood samples were obtained form individuals after taking informed consent on the condition that each of these individuals had at least one first-degree relative affected with FH. Genomic DNA was isolated, exon-specific intronic primers were designed and used to amplify DNA samples from individuals.PCR products were directly subjected to automated DNA sequencing to detect the mutations. Along with the affected individuals, ten ethnically matched controls were also analyzed to determine the presence of the same mutations. Patients with Nephrotic Syndrome admitted to hospital were excluded from the study.*

Results: *All the 24 patients had total cholesterol level above 300 mg/dl and LDL cholesterol level above 200mg/dl. Sequence analysis of the LDL receptor (LDLR) gene showed 3 novel mutations which have never been reported elsewhere. In exon 10 we reported g.29372_29373insC, which was found in all the 24 patients and was missence mutation coding for C (cysteine) instead of V (valine).*

Conclusion: *Our study reported 3 novel mutations in 24 Indian families. These novel mutations are predicted to produce change in the amino acid and thus leading to the conformational changes in the structure of LDLR protein. Change in the LDLR protein makes the LDL receptor unable to transport the cholesterol in to the cell and hence cholesterol starts accumulating in the blood stream and leads to FH.*

Key Words: *Familial Hypercholesterolemia; Mutation analysis; LDL Receptor gene*

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