Name of the scholar: YASER SIAHBALAEI

Name of the Supervisor: Prof. Arif Ali

Name of the Co-Supervisor: Prof. Kuljeet Singh Anand

Name of department: Biosciences

Topic: Study of polymorphism of IDE gene in Alzheimer disease & diabetes, expression of amyloid beta (Aß), elucidating the role of IDE in Indian Subpopulation

Abstract

The population of older people is on the rise worldwide. Although today's number of older people are higher in more developed nations, the fastest rise in this group is happening in the less developed world. Life expectancy in India has risen from 37 years in 1950 to 65 years in 2011, and by 2050, lifespan is expected to reach 74 years.

The WHO has reported that the occurrence of non-communicable or chronic diseases (NCDs) are rising as the population ages. United nation 2015 projected that in next decade, the major health threats globally will be greater from the NCDs (e.g., diabetes, heart disease, mental illness, cancer, and arthritis) than from infectious and parasitic illnesses, childhood disorders, and accidents which were mains health threats traditionally, and in India these problems are more noticeable, because of its huge population. Meanwhile, data from India's National Sample Survey (NSS) reported the positive association between mental disease incidence and age, especially in rural areas. This demographic shift poses enormous and complex challenges to Indian society in the form of an increasing burden of NCDs.

One of the ways to address this problem is to try to improve our understand of the association between age and health through research in order to reach to its root cause and unrevealed the mechanisms behind the NCDs which is one of the main problem faced by elderly individuals of the population. This study focuses on two very important NCDs, which are: Type 2 diabetes mellitus (T2DM) and Alzheimer disease (AD). These are diseases of old age and I have made an attempt to establish a link between them by studying the relationship between gene polymorphism and the protein marker on the plasma of patients suffering these diseases.

In order to establish interrelationship between T2DM and AD, which is part of this Ph.D. dissertation, a thorough literature review was conducted to locate the key mechanism which played certain role in both diseases; and after the literature search in this area, I found that one of the links between T2DM and AD, was their key catalytic enzyme, insulin degrading enzyme (IDE). Polymorphism study is in or near IDE gene has been associated with variation of insulin and Ab levels in plasma. Mutations at the IDE gene locus, in the rodent model of T2DM, has been shown to be linked to DMs susceptibility, leading to rising in blood glucose and insulin levels.

This thesis consists of a series of three experimental studies, each of which focusses on one area of better understanding the relationship between AD and T2DM. Several polymorphisms of IDE gene and plasma amyloid beta levels affect shaped this both diseases. The overarching goal of the current research is to investigate how several modifiable and non-modifiable factors affect these two diseases. These include factors associated with health risk (i.e., blood pressure, PP, BMI, plasma amyloid beta 42 levels, gender, food habit, education, MMSE, plasma lipid profile, plasma blood cell accounting) and genetic risk (i.e., ApoE and IDE). The primary aim of this thesis is to examine (a) the independent effects and (b) the interactive effects of health conditions (i.e., PP, blood pressure and BMI and plasma amyloid beta levels and gender, food habit, education, MMSE, plasma lipid profile, plasma blood cell accounting, sugar levels) and genetic polymorphisms (i.e., ApoE, IDE) on the diseases in older adults (aged 60-95 years). Answers to these general aims produce a picture that will help adults make health and lifestyle choices or changes that could translate to better-continued quality of life into old age.

The objective of present work was to find out whether Insulin Degrading Enzyme (IDE) polymorphisms have any association with Alzheimer disease (AD) and Type 2 Diabetic Mellitus (T2DM) and Alzheimer plus Type 2 Diabetic Mellitus (A/D) patients, reflected in ApoE polymorphism and Amyloid Beta 42 (Ab 42) protein. From this investigation, it would also be possible to identify any geographic genetic variation in Indian (Asian) population by comparing obtained results with the findings from the published study on other part of the world populations.