(International Print/Online Journal)

SJIF IMPACT FACTOR: 4.617
GADIF IMPACT FACTOR: 1.49

ISSN (Print): 2209-2870
ISSN (Online): 2209-2862

International Journal of Medical Science and Current Research (IJMSCR)
Available online at: www.ijmscr.com
Volume2, Issue 1, Page No: 04-08
January-February 2019

IJMSCR

Gene-Environment Interaction in Type II Diabetes

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Type of Publication: Original Research Paper
Conflicts of Interest: Nil

ABSTRACT

Type 2 diabetes is a significant and fastest growing public health problem all over the world. The development of type 2 diabetes is associated with environment as well as genetic factors. Various clinical studies and prospective studies have found that gene-environment interaction can result in the development and progression of type 2 diabetes. This study has significantly focused on identifying the interaction between gene-environment interaction and how this interaction results in the development of type 2 diabetes. In the past decades, the studies conducted have mainly focused on analysing the traditional link between the genetic factors and occurrence of type 2 diabetes. For this purpose, this study provides a comprehensive review of literature and concludes that interaction between environment factors and genetic factors can be very significant in understanding the occurrence and consequences of type 2 diabetes. The environment factors are also considered as the non-genetic factors, which interact with genetic factor and increases the prevalence of the disease. Also, the study identifies that genetic factors are not alone and responsible for the development of disease, but interaction with various environment and lifestyle factors are also responsible for type 2 diabetes.

Keywords: Diabetes, gene-environment, life style, clinical studies, environmental factors, non-genetic factors, genetic factors.

INTRODUCTION

Diabetes mellitus is a chronic disease that claims many lives and causes significant level of morbidity among the population. Evidences have shown that diabetes is the oldest disease known to man, as it has been found to be written in the Egyptian manuscript from 3000 years ago [5]. Diabetes is of two kinds- Type 1(insulin dependent) diabetes and type 2 diabetes (non-insulin dependent). Type 2 diabetes is considered as the most common form of diabetes that affects most of the population suffering from diabetes mellitus. Type 2 diabetes is characterized with insulin resistance, hyperglycaemia and relative deficiency of insulin. The main causes of type 2 diabetes are interaction between behavioural, environmental and genetic factors. People suffering from this chronic condition are also considered as highly vulnerable to various, short- and long-term complications which can also lead to significant morbidity and premature death among individuals. The commonness of the type 2 diabetes is the major reason of high morbidity and mortality and also insidious onset and late identification of disease also increases the severity of the disease.

Various studies have informed about the gene-environment interaction as the major risk factor of increasing prevalence of type 2 diabetes. Gene-environment interaction is considered as the combination of the genetic and environmental factors that contribute to the occurrence of type 2 diabetes. There are certain genes in the individuals that enhance the susceptibility of the disease, but they are not sufficient to produce diabetes. This also means that there are certain genes that can increase the susceptibility to diabetes by compromising insulin secretion or insulin action. However, the clinical identification or recognition of the disease may not be possible, till certain threshold is exceeded. Some

of the common environmental factors that increases the risk of diabetes are sedentary lifestyle, obesity, high-fat diet or lack of physical activity, which may result in compromising insulin secretion and insulin action. These environmental factors in the individuals with susceptible genes can interact and can cause diabetes.

This interaction has become a major problem, as it results in increasing the prevalence of type 2 diabetes, increasing the rate of morbidity and mortality and increasing healthcare and financial burden. Therefore, the main aim of this research is to understand that what is gene-environment interaction and how it is mainly associated with the occurrence of type 2 diabetes. The research will provide a comprehensive set of current evidences that suggest that how understanding this interaction can help in reducing prevalence of type 2diabetes.

Gene Environment Interaction in Type 2 Diabetes

Type 2 diabetes is considered as the multi-factorial disease; however, the causes of type 2 diabetes can vary from genetic to environmental [1]. Type 2 diabetes has also become a global health crisis, because of the rate of morbidity and mortality associated with it. The study conducted by Jyothi & Reddy [2] has found that 95% of the population suffering from diabetes constitutes of those suffering from type 2 diabetes. Studies have also identified that sudden increase in the prevalence of type 2 diabetes and its epidemic level primarily the major consequence of some of the recent changes that occurred in environment [2]. In the recent years, scholars have also started focusing on the problem of gene-environment interaction, which is also considered as the "*intrauterine environment such as intrauterine growth restriction result in gene expression changes in various tissues, which ultimately lead to the onset of diabetes*" [3] (p. 7). It has also been identified that the population level genetic changes take many generations to occur and are not very quick, therefore, the reason of epidemic of type 2 diabetes is mainly because of the recent changes in the environment.

Though, diabetes is the disease that mainly occurs in the genetically predisposed population [3], which also means that effects of the pre-existing susceptibility genes has been triggered by the non-genetic environmental factors. Studies have identified that predisposition in the population is also influenced by the certain level of exposure to the environment, genotype, personal and lifestyle factors and also level of access to good quality primary care [3, 4]. Franks, Pearson & Florez have also informed that the interaction between the genetic and on-genetic risk factors can result in increasing the prevalence of type 2 diabetes and raise the risk of diabetes in synergic manner. Therefore, the changes in the sedentary lifestyle, health improving behaviour of the individuals, enhancing compliance to medication and reducing the risk from environmental factors [5]. Developing an understanding towards these interactions can be significantly effective in identifying various ways of conducting a reliable observation gene-environment interaction in healthcare setting [6].

The definition of gene-environment interaction has been found to vary with the field of diabetes research, yet the epidemiological definition of this interaction can be adopted for the purpose of this research. The interaction is also called as the effect modification or effect modulation. Study has identified "*for binary outcomes, an interaction would be present if the combined risk attributable to genetic and environmental exposures is significantly greater or less than expected if their effects were additive*" [5] (p. 1414). It has also been found that for the quantitative traits the various genetic effects can differ on the range of environmental factors, the word environment in the term "gene-environment interaction" is mainly associated or related to all the non-genetic factors to which individuals are often exposed. The environment can extend from macro to micro and has also been related to the lifestyle behaviours [6]. The word interaction is therefore, used to display and inform about the joint effect of the genetic characteristics and second factor that is responsible for the occurrence of the type 2 diabetes. In the case of interaction genetic exposure is significantly associated with environment factors.

How Gene-Environment Interaction is Responsible for Type 2 Diabetes

Type 2 diabetes is becoming the fastest and growing health problem for the people all over the world. The number of people suffering with type 2 diabetes has increased to millions [6]. Type 2 diabetes has been a major problem and a significant issue identified in

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this research because it has been identified that type 2 diabetes earlier affected people from middle or older age, however now it has also become prevalent among children and adolescent resulting in a significant burden of disease [7]. Environmental factors are considered as the major reason behind the prevalence of type 2 diabetes, such as obesity (which is also affecting children in very young age), physical inactivity among the adults due to busy schedules, lack of participation in physical exercises and activities resulting in increasing weight [8], changing eating pattern and type of food (high calorie food intake) and also sometimes due to lack of resources (such as in developing nations like Africa [8].

The genetic factors in diabetes are considered as one of the main risk factors. Genetics is associated with the genes and studies informed that family history of type 2 diabetes, as well as the history of disease in the first-degree relatives can increase the risk of type 2 diabetes to three times in the individuals. This is mainly related to the genes that family members share. Therefore, type 2 diabetes is associated with strong genetic component [8]. Type 2 diabetes is therefore, associated with heritable genetic correlations. Some of the studies have found that strong evidences about the significant genetic components in type 2 diabetes [9, 10]. 40% population develop type 2 diabetes due to heritable genetic components, while only 6% general population have the chances of developing type 2 diabetes. Therefore, according to these evidences, there is a strong relation between environmental and genetic factors with development of type 2 diabetes. However, the interaction between the environmental and genetic factors increase the chances of this chronic disease.

The development or the occurrence of type 2diabetes can be understood through environment and gene interaction. According to evidences provided in the study of Cornelis [11] there are some genes in the individuals who are at the higher risk of diabetes that are susceptible to diabetes, but they are alone not able to develop diabetes these genes may remain dormant till the time they interact with other risk factors, such as environmental factors [12]. This is the main reason that diagnosis of the type 2 diabetes can be delayed. The genes in the individuals that are more susceptible to diabetes can result in compromising insulin action or insulin secretion. The environment factors, such lack of physical activity, intake of high calories diet and obesity. Studies have also identified that environment factors can also directly compromise with insulin action and insulin secretion and the interaction of genetic factors and environmental factors can result in diabetes. The risk of diabetes significantly increases with this interaction [13].

A study conducted by Esparza-Romero et al [14] has identified the significant role of environment factors in increasing the prevalence of type 2 diabetes. More than half of the population of Pima Indians of Arizona are affected by diabetes and the identification of the disease is mainly found in the age of adolescence [14]. The main reason of the occurrence of type 2 diabetes that has been identified in the literature is that the people earlier had more effective and active lifestyle, which reduced over the period. Most of the indigenous population all over the world, suffers from type 2 diabetes because they had a hunter-gather lifestyle (some times also suffered from frequent famine) and became susceptible to the adverse effect of industrialized environment [15]. This change is called as "thrifty genotype hypothesis". However, it has been identified that "*the original description of the thrifty genotype hypothesis focused on the over-production of insulin after meals and a corresponding period of hypoglycemia that induces appetite, the idea that efficient storage and utilization of energy in adipose tissue is a selected trait has also been widely discussed and attributed to thrifty genes*" [16] (p. xii).

Gene-lifestyle interaction and its association with type-II diabetes

Gene-lifestyle interaction is considered as the interaction between genetic and lifestyle factors. A study has identified that type 2 diabetes affect around 382 million people worldwide. The disease mainly affects the people living in developing nations. Studies have identified that type 2 diabetes develop with the interplay between the genetic and lifestyle factors [17]. Therefore, the current researchers focus on developing the lifestyle interventions, because it has been found that lifestyle interventions can significantly reduce the risk of progression of type 2 diabetes, even in the high-risk individuals. The consequences of the adverse lifestyle factors also differ with the underlying genetic factors [18]. Gene-lifestyle interaction has also been studies in the

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context of metabolic diseases and cardiovascular disease, which are also significant chronic disorders like diabetes. Many cohort studies and case control studies were published in 1990's. Ge that have identified the significant interaction between gene and lifestyle. Aschard et al [19] in their study has made many assumptions regarding the frequency and magnitude of interaction effects about various common diseases and common exposures. The study also identified that there is a significant relation between the genetic factors and the lifestyle factors.

The lifestyle factors can be associated with the physical activities, diet, smoking, toxins and pollutants [20]. Gene lifestyle interaction can also be associated with obesity. Obesity is the problem associated with being overweight. Being overweight can be a significant problem in adults as well as in children. The lifestyle factors associated with obesity are again physical inactivity, imbalanced diet, high calorie food intake, eating disorders and genetic factors. Therefore, the influence of the adverse lifestyle factors results in susceptibility of type 2 diabetes. Therefore, the studies have identified that genetic and lifestyle factors are significantly associated with the higher risk of type 2 diabetes [20]. The various other lifestyle factors are sex, physical activity, diabetes family history and dietary habits. Therefore, the lifestyle interventions can significantly address the negative consequences of interaction between genetic and lifestyle factors [21].

Conclusion

Type 2 diabetes is a very significant and chronic disease that affects the health and quality of life of many people all over the world. Type 2 diabetes is considered as the multifactorial disease, which means it is related to many environment and genetic factors. The interaction between these factors result in bringing the changes in gene expression. Type 2 diabetes have been found as the major health problem because it has reached to epidemic level all over the world. Earlier type 2 diabetes, which is also considered as non-insulin dependent was mainly associated with the genetic factors and to a limited environment factor. However, according to the current research and evidences, the occurrence of type 2 diabetes among the population is also associated with environment and behavioural factors. The evidences identified in this research has informed that there are various factors that are associated with occurrence of type 2 diabetes and one important factor is gene-environment interaction.

The main focus of this research is mainly on understanding the interaction between genetic and environment factors. This focus has been placed because the studies have identified that genetic changes that could lead to the occurrence of type 2 diabetes can take many years, while other studies have shown that prevalence of type 2 diabetes has been increased over the years and more people in the developed and developing nations are being suffered from type 2 diabetes. Therefore, this research identified that interaction between the genetic and environment factors have been significantly associated with type 2 diabetes. The research concludes that gene-environment interaction can significantly increase the chances of progression of type 2 diabetes. The findings of this research also inform that gene-environment interaction could provide some detailed insight to the mechanism and the risk factor that contribute to the disease. This could also be helpful in developing various effective interventions in order to reduce the prevalence and severity of type 2 diabetes among population.

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