Current Views on the Significance of Genetic, Dietary and Behavioural Factors in the Development of Type 2 Diabetes Mellitus

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Abstract

The global prevalence of type 2 diabetes mellitus have been on the increase and by no means slowing down. And this have heap huge medical expenses on countries across the world, as it's now more frequent in both adults and children. In this view, this article is timely to provide insight on how to best prevent or delay the onset of type 2 diabetes mellitus. Much more, to create awareness of genetic predisposition, having a healthy diet and regular exercise in a changing world that is obesity prone.

Keywords: Diabetes; Type 2 Diabetes Mellitus; Dietary Factors; Genetic Factors; Smoking

Introduction

Type 2 diabetes mellitus (T2DM), is of wide occurrence [1] and the predominant form of diabetes mellitus [2,3]. It is estimated that 300 million will be diabetic by 2025 [2,4,5]. The T2DM prevalence or incidence is escalating worldwide owing to major changes from traditional indigenous diet to a typical 'Western' diet. Furthermore, the shifting/changing of lifestyle from agrarian existence to city living, which involve lesser physical activity has also contributed to T2DM's escalation [3,6,7]. T2DM also referred to as non-insulin dependent diabetes mellitus, NIDDM [3,8] involves many different elements that act in concert to cause the disease. As such, it may result in severe complications including retinopathy, nephropathy and neuropathy [9,10]. Also, a risk factor for coronary heart disease [11,12]. Thus, T2DM is said to be complex heterogeneous group of metabolic disorders including hyperglycemia and impaired insulin action and/or insulin secretion [2,8,13]. Here, the importance of genetic, dietary and behavioural factors to the mechanisms and development of T2DM is being considered.

Diabetes mellitus simply is a systemic disease in which the body experiences an impairment syndrome specifically to glucose metabolism, which then leads to a series of disorders in both protein and lipid metabolism [2]. Diabetes mellitus occurs in varied types but two most common forms are type 1 and 2 [8]. Type 1 diabetes- involves reduced production of insulin, and type 2 diabetes- involves impaired response to insulin and β-cell dysfunction [2,8,13,14]. Both are characterized by glucosuria, frequent urination, hyperglycemia, compensatory thirst, blurred vision, increased fluid intake and changes in energy metabolism [13]. Therefore, to understand T2DM better, it's imperative to explain the metabolic changes that occur in its developmental stage. Physiologically, insulin is constantly synthesized by the pancreatic β-cells, regardless of blood glucose levels, although it is stored in vacuoles until it's needed [13]. Insulin is the principal hormone that regulates uptake of glucose from the blood into most cells, including skeletal muscle cells and adipocytes [2,13,15].

Insulin's release is triggered by the changes in blood glucose level thus converting glucose to glycogen for storage in liver and skeletal muscle cells [8,13]. However, in the event of viral infection or autoimmune disease of β-cells insulin resistance is developed [3,10]. Insulin resistance is defined as the suppressed or delayed response to the action of insulin [3]. In the light of insulin resistance, β-cells increase insulin output in order to establish and maintain a normal blood glucose level [3,4]. Although, the persisting effect of insulin resistance and hyper secretion of insulin, if not reversed progresses to states of impaired glucose tolerance (IGT) and impaired fasting glycaemia [3]. Further progression leads to T2DM (Figure 1) [3].

Figure 1 clearly depict that insulin resistance results from interaction between genetic and environmental factors [3,7]. Though, T2DM is a complex multifactorial disease as shown in figure 2, which makes it, difficult to it's a etiology [13]. However recent studies have shown the influences of genetic, dietary and behavioural factors on T2DM [3,16,17].

Genetic Predisposition

The fact that T2DM is a genetic disease has been established [6,7,13,16]. As evidence has it that the chances of T2DM in monozygotic twins is about 70% compared with 20% to 30% in monozygotic twins is about 70% compared with 20% to 30% in any medium, provided the original author and source are credited.
dizygotic twins [6] and also that T2DM clusters in families [3,6]. Though, the genetic complexity of T2DM has been limited to unraveling susceptibility to T2DM [3,7]. Until 2007, only three genes were consistently associated with T2DM: PPAR-gamma (PPARG), potassium inwardly rectifying channel subfamily J member 11 (KCNJ11) and transcription factor 7-like 2 (TCF7L2) [6]. The PPARG gene can be helpful in predicting future T2DM especially in individuals with a Body Mass Index (BMI) > 30 and fasting plasma glucose > 5.5mmol/L [6,16]. KCNJ11 regulates trans membrane potential and thereby glucose-stimulated insulin secretion in pancreatic β-cells while TCF7L2 is much involved in proliferation of β-cells in response to increased demands [6,16]. Considering the breakthrough those genetic variants of T2DM would bring to the understanding of path physiology of T2DM and the management of the disease is promising. Even now that, genome-wide association studies have identified more genetic variants associated with T2DM [6,13,16].

In view of these advances, insight into the relevance of genetic determinants to medical therapy (pharmacogenomics) based on an individualized genetic variants sequence, the propensity to develop diabetes-related complications and mediators of gene-environment interactions can be achievable [6,18]. Hopefully, this approach will expose the potential risk of T2DM, thus, help to provide the necessary care at the early stage, thereby reduces medical expenses accompanying the later stage treatment of T2DM. Owning to the fact that T2DM is on the increase in different countries across the world and this is causing financial burdens [18]. Hence, it would be necessary to consider the significance of genetic

Figure 1: Developmental stages of type 2 diabetes mellitus and its risk factors (Steyn et al. 2004)

Figure 2: Pathogenesis of type 2 diabetes mellitus (T2DM). This include a defect in insulin-mediated glucose uptake in skeletal muscle, a disruption of secretory function of adipocytes, a dysfunction of pancreatic β-cells, impaired sensing and response to hyperglycemia in the central nervous system (CNS), an excessive accumulation of lipids and impaired fatty acid oxidation due to obesity, physical inactivity and genetic predisposition (Lin & Sun, 2010).
and the rapid occurrence of T2DM; as some diet aspects are the main causative of T2DM [3,4,7,8,20].

Both glucose tolerance and insulin sensitivity were modified with dietary fat consumption. It was found that high-fat diet alleviates insulin resistance [3,20] which is abundant in the western diet compared to the indigenous diet thus, a plausible explanation for the escalation of T2DM in the developed countries. Although it’s now known that some Fats are beneficial. Fats like poly unsaturated fatty acid (PUFA) and higher vegetable fat (unsaturated fat) are associated with a lower risk of T2DM [8]. However, it’s advisable to reduce fat intake in general, in order to reduce energy intake because all fatty acid eventually contribute to excessive accumulation of triacylglycerol, diacylglycerols and ceramides in the sarcoplasm of skeletal muscle [13,14,21]. These then leads to obesity (Figure 2) and further into T2DM [4,21]. Precisely, total fat intake should be 30% of energy intake, with no more than 10% from saturated fats and also, averages intakes of 6% of energy from PUFA and 12% from mono unsaturated fatty acid (MUFA) [8].

On the other hand, carbohydrate has low risk to T2DM [3]. But due to the fact, it has a calorie value and also its eventual breakdown product is glucose [14]. Its intake should be minimal otherwise leads to obesity syndrome [22]. Glycaemic index should be noted here. GI can be defined as the measure of the post-prandial glucose response after carbohydrate consumption [3]. Since there are considerable differences in the physiological responses to different form of carbohydrate, thus there is high and low GI. Carbohydrate, for example, sugar that gives a high GI result to increased lipogenesis and secretion of very low density lipoprotein (VLDL) from the liver [8]. VLDL eventually produce low density lipoprotein (LDL) which has a high cholesterol content and invariably causes insulin resistance as shown in Figure 2 [13].

Hence to avoid T2DM, carbohydrate with high dietary fiber content should be consumed because high dietary fiber diet have been shown to lower post-prandial glycaemia and insulin levels [3,8]. Dietary fiber is made up of non-starchy polysaccharides (NSPs), plus lignin, oligosaccharides and resistant starch [3]. It’s found that NSPs in an average British diet is between 11g and 13g/day which is low compared to the recommended average intake - 20g/day [8]. Thus, diseases like constipation, hemorrhoids and straining while defecating is common in this part of the world because dietary fiber eases bowel movement in the gut [3,8]. Examples of dietary fiber-rich foods are whole grain cereals, whole meal cereal products, fruit and vegetables. Furthermore, diets rich in fruits and vegetables reduces the risk of T2DM [20] owning to its dietary fiber content. Also it’s an antioxidant supplement [8]. In addition, protein is also beneficial to the body as its breakdown product can be reused in the fasting state. However, excessive high intake is associated with high risk incidence of T2DM. Thus, intake should be moderate (Figure 3) [22].

![Figure 3: The Eatwell Guide (FSA, 2016)](image-url)
It is in this view that changes in the average western diet were made and summarized in Figure 3 based upon recommendation by nutritionist and medical scientists [22]. Though there is still the question of what kind of diet best prevents T2DM [1].

3.3 Behavioural Factors

Many epidemiological studies have indicated the importance of behavioral factors to the development and underlying metabolic activity of T2DM [3,4,7,13]. The factors are: cigarette smoking, alcohol consumption and physical activity. Since, studies have shown that there is genetic predisposition to T2DM and genetic make-up cannot be changed, then, the obvious decision is to alter environmental factors (lifestyle manipulation) that alleviate T2DM occurrence. Thereby, this should slow the onset of T2DM. Also, this approach will be beneficial to individuals not prone to T2DM. Thus, behavioural factors are of high significance as shown hereafter.

It has been pointed out that cigarette smoking is considered to increase the risk of diabetes [4,23]. Smokers tend to have higher glycosylated hemoglobin (HbAlc) concentration, especially heavy smokers [4,23]. HbA1c is considered a long-term marker for glucose homeostasis, its depict the average blood glucose concentration ranging from 2-3 months [23].

Consequently, strong association exists between daily physical activity and T2DM [4,24]. Individuals with T2DM that live physically active lifestyle (exercise) show improvement due to their treatment. Likewise, individuals with IGT eventually did not develop T2DM. Although, it’s important to adhere to recommendation on how to quantify the intensity and duration of the exercise involved. Regarding alcohol consumption (moderate intake), it’s associated with reduced incidence of T2DM [3,8]. But there is some inconsistency on gender issue. Apparently, in a particular study, men show significance increase in T2DM incidence despite having more than 21 alcoholic drinks per week while in the women, no association was found between T2DM and alcohol intake [3]. Thus, opinion differs as to whether the protective effect of modest alcohol consumption is due to the alcohol itself or some other constituent of alcoholic drinks [8]. But for the fact that the same protective effect is exhibited by red wine and some dealcoholized wine, an indication that alcohol is not the protective factor. So, the possibility is shifted to polyphenols in red wine because of its antioxidant action [8].

In the light of above evidence, consumption of moderate to average alcohol intake is recommended. Furthermore, a study shows that it lowers glycaemic load in a low risk group of T2DM [4]. Thus, abstinence from alcohol is associated with an increase in the risk of diabetes. However, recommendation is strongly advised to be given and comply with, because habitual excess consumption of alcohol is associated with long term health problems like mental deterioration, liver damage, hypertension and cancer of the oesophagus [8].

**Conclusion**

The significance of genetic, dietary and behavioural factors to the development of T2DM and its underlying mechanism of action make a compelling case for its management and prevention. Recently, there has been sizeable amount of evidence showing the potentially preventable nature of T2DM, particularly in the combining genetic, dietary and behavioural (lifestyle) interventions in delaying or reducing T2DM.

Therefore, health policy makers need to plan in motion to utilize the above factors. Furthermore, the populace need to be informed of a lifestyle of regular exercise, adhere to weight control measures via eating healthy food as exemplary in UK ‘change4life’ and Finland ‘DEHKO’ project [25].

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**References**