Understanding the causes of diabetes and its complications

Abstract

Diabetes mellitus (DM) has become a great global health issue and constitute a major burden on the global healthcare system including both the Western and non-Western nations. The global prevalence of DM is now put at 415 million people (8.8% of the world population) while the total health expenditure of DM is now estimated at 673 billion dollars with.1 Among the various classes of DM, type 2 DM (T2DM) has become the most widespread due to the alarming geometric increase in obesity, poor diet and the low physical activity lifestyle.2,3 Furthermore, one of the most serious microvascular complications of diabetes mellitus is diabetic nephropathy (DN). The disease has not only become the leading cause of chronic kidney disease and end-stage renal disease (ESRD) globally but also associated with increased cardiovascular mortality. Almost 50% of patients starting renal replacement therapy in some Asian and European countries, as well as the US, have been primarily diagnosed with DN with Asians having the highest prevalence of nephropathy.4,5

About 30–40% of patients with both type 1 and 2 diabetes develop DN. Clinically, persistent microalbuminuria, as well as the gradual decline of the kidney function which eventually leads to ESRD, underscores DN. A strict control of blood glucose and blood pressure, as well as renin-angiotensin system blockade, remains the most current treatment strategies of DN. These, however, only slow down but not arrest the progression of DN. The fact remains that the etiology of DN is multifactorial and polygenic, generally including both genetic and environmental factors.6 In other words, both conventional modifiable risk factors (such as hemodynamic changes, hypertension, hyperlipidemia, and smoking,) and non-modifiable factors (such as race, sex, and genetic background) contribute to an inherent susceptibility to this disease. The genetic basis of DN is, however, heterogeneous.7

Family aggregation is clear evidence supporting the role of genetic susceptibility to the development of DN. More importantly, not all patients with diabetes develop clinically evident DN despite long-term poor glycemic control.8 One of the approaches commonly used to dissect the mechanisms of onset and progression of DN is through identification of susceptible genetic loci or genes. Unfortunately, there are always inconsistencies in the association of the various loci or genes to DN. This does not only make these loci or genes unable to account for a significant proportion of the heritability of DN but also indicate the existence of factors beyond genetic sequence variations. A rapidly evolving field in the past decade is epigenetics which is mainly related to the alternations in gene expressions through regulatory mechanisms that include DNA methylation, histone modifications as well as expression of noncoding RNAs such as microRNAs (miRNAs).9

In conclusion, the environmental, genetic and epigenetic factors should be considered in understanding the pathogenesis and in proffering solutions and treatment to diabetes and its complications.

Introduction

Diabetes mellitus (DM) is one of the long-standing metabolic diseases that has not only become a great global health issue but also constitute a major burden on the global healthcare system including both the Western and non-Western nations. The global prevalence of DM is now put at 415 million people (8.8% of the world population) while the total health expenditure of DM is now estimated at 673 billion dollars with.1 Among the various classes of DM, type 2 DM (T2DM) has become the most widespread due to the alarming geometric increase in obesity, poor diet and the low physical activity lifestyle.2,3 Furthermore, one of the most serious microvascular complications of diabetes mellitus is diabetic nephropathy (DN). The disease has not only become the leading cause of chronic kidney disease and end-stage renal disease (ESRD) globally but also associated with increased cardiovascular mortality. Almost 50% of patients starting renal replacement therapy in some Asian and European countries, as well as the US, have been primarily diagnosed with DN with Asians having the highest prevalence of nephropathy.4,5

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In conclusion, the environmental, genetic and epigenetic factors should be considered in understanding the pathogenesis and in proffering solutions and treatment to diabetes and its complications.

Acknowledgments

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Conflicts of interest

Authors declare that there is no conflicts of interest.

References