Clinical Complications of Type-2 Diabetes Mellitus in South Asian and Chinese Populations: An Overview

Gundu H R Rao1*, Pratiksha G Gandhi2 and Vineeta Sharma3

1Emeritus Professor, Laboratory Medicine and Pathology, University of Minnesota, USA
2Chairperson, IPC Heart Care, Mumbai, India
3Molecular and Cell Biologist, San Francisco, California, USA

Abstract
According to recent projections of World Health Organization (WHO), India already leads the world, with the largest number of diabetic subjects. China is fast approaching to claim the number one spot. World Diabetes Federation estimates, that India has over 65 million diabetics and an equal number of pre-diabetics. Major contributors for the development of this chronic disorder are hyperglycemia, insulin resistance, dyslipidemia, hypertension, endothelial dysfunction, obesity, oxidative stress, and metabolic syndrome. Some of the early symptoms related to this altered glycemia include polydipsia, polyphagia, polyuria and changes in the vision. Later clinical complications include vasculopathy, peripheral neuropathy, nephropathy and pre-disposition to infections. Clinical trials have demonstrated the benefits of tight control of hyperglycemia as well as of multiple risk factors. Early detection of hyperglycemia, insulin resistance, altered lipid metabolism and better management of these observed risks, is the best choice we have, to reduce the Global Health Care burden. Excess glucose in the circulating blood seems to impair the endothelial dependent vasodilatation in both the microcirculation as well as macro-circulation. Prolonged exposure to hyperglycemic environment and altered endothelial function seems to accelerate the pathogenesis of atherosclerosis and type-2 diabetes and its clinical complications.

Keywords: Hyperglycemia; Hypertension; Obesity; Endothelial Dysfunction; Metabolic Syndrome; Insulin resistance; Type-2 diabetes; Platelet hyper function; Gene therapy

Introduction
South Asians (Indians, Pakistanis, Bangladeshis and Sri Lankans) have very high incidence of Cardio Metabolic Disorders (CMDs), such as hypertension, atherosclerosis, central abdominal obesity, metabolic syndrome, Type-2 Diabetes (T2D), coronary artery disease, and stroke [1-3]. According to World Diabetes Federation currently we have over 65 million diabetics and an equal number of pre-diabetics. India and China are in race for the first place in number of diabetics. In spite of the fact that large numbers of individuals are at risk, according to reliable sources, 50-70% of the subjects in China and 30-80% of the individuals in India are not diagnosed and are therefore left untreated. This is to a large extent due to lack of public awareness and limited opportunities for diagnosis. World Health Organization prediction of losses in national income for China exceeds USD378 billion and for India, USD237 billion (www.cadiresearch.org). To a great extent the increase in the incidence of type-2 diabetes, is attributed to the changes in the life-style, diet, lack of physical activity that promotes obesity. Although type-2 diabetes has increased significantly over the years in China and India, it continues to increase at a fast rate in the USA, as well as other countries across the world. In other words, the world epidemic of type-2 diabetes is affecting both the developed and developing countries. Vascular complications related to diabetes accounts for the majority of economic burden worldwide. About one half of the diabetics die prematurely due to cardiovascular complications and a tenth due to renal failure. In spite of the fact that there is an increase in the incidence of this disease worldwide, the major share of the morbidity and mortality is predicted to occur in the resource poor countries. Various risk factors that contribute diabetes and vascular disease are known. Although these risks are modifiable or preventable, there are very little efforts in progress in majority of the developing world, to monitor or control them. Known risks include, impaired insulin secretion, insulin resistance resulting in hyperglycemia. Some of the early symptoms related to this altered glycemia include polydipsia, polyphagia, polyuria and changes in the vision. Later clinical complications include vasculopathy, peripheral neuropathy, nephropathy and pre-disposition to infections. Other than the earlier symptoms, the only diagnosis used by and large, is measuring plasma glucose or glycosylated hemoglobin. Management is through lifestyle changes, diet modifications, exercise, drugs that modulate the blood glucose levels. Clinical studies have demonstrated that adequate glycemic control reduces the clinical complications associated with this disease. We strongly believe, that the early detection and better management of the observed risks, is a better choice to reduce the economic burden of this disease worldwide. In this overview, we will discuss the clinical complications associated with these chronic metabolic diseases and suggest some ways, to better manage the observed risks.

Fetal Origin of CMDs
Since we firmly believe, that the early detection of the risks for CMDs and effective management of the risks is the best choice we have for reducing the Global burden of these metabolic diseases, we will have to start our prevention strategies at the earliest. What is the earliest stage that we can start prevention strategies? According to the seminal epidemiological work at the Mission Hospital, Mysore, India, thirty

*Corresponding author: Gundu H R Rao, Emeritus Professor, Laboratory Medicine and Pathology, University of Minnesota, 420 Delaware St SE, Minneapolis, Minnesota 55455, USA, Tel: 952 594 5248; E-mail: gundura09@gmail.com

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percent of the children born in India, are of low birth weight. The birth record of all the children born in this hospital is maintained from 1936. In view of this meticulous record keeping, Medical Research Council (MRC) of UK has set up an epidemiology wing at this hospital. Studies from this group on "Mysore Cohort" for decades, have established that these children as they grow up have a higher risk of developing metabolic diseases, such as hypertension, obesity, metabolic syndrome, heart disease and stroke [4-12]. These findings are not unique to South Indian children. Studies on the effect of low birth weight on the development of metabolic syndrome, has been investigated in the Fetal Origin of Adult Disease (FOAD) "cohort" of Beijing, China [13-15]. Several studies have demonstrated fetal origin of metabolic diseases and supported the thrifty phenotype hypothesis of Barker, which proposes that survival physiology and metabolism are altered under condition of poor fetal nutrition, as an adaptive response, these alterations affect the long term metabolism of these cohorts.

Excess Weight and CMDs

According to National Institutes of Diabetes, Digestive and Kidney Diseases of National Institute of Health, USA, approximately two-thirds of all adults in the USA (167 million), are overweight and a third are obese. The WHO estimates that there are 1.3 billion overweight adults globally. Of these 300 million are clinically obese. According to National Health and Nutritional Examination Surveys (NHANES I, 11,111) the crude prevalence of excess weight and obesity (BMI>25.0) for those aged>20 years was 59.4% for men and 54-9% for women. Obesity is an important modulator of various risks associated with vascular diseases, including insulin resistance. The association of excess weight with type-2 diabetes and insulin resistance is well recognized [16]. Insulin resistance is also linked with a variety of associated risks including hypertension, hyper-lipidemia, atherosclerosis, metabolic syndrome, and endothelial dysfunction. However, not every obese individual will have insulin resistance. Furthermore, there are millions of lean subjects who have insulin resistance. The specific mechanism by which enlarged adipose tissue induces systemic insulin resistance is not known.

South Asians have a high incidence of T2D and cardiovascular disease, despite a low prevalence of obesity. Based on a collaborative study done at the Madras Diabetes Research Foundation (MDFR), Chennai, India, and the staff of University of Minnesota, a hypothesis was developed to explain the increased burden of T2D in this population. They hypothesized, that the increased risk might be due to a high propensity towards the abdominal fat or visceral fat accumulation in the South Asian population. To account for the differences in body size and general adiposity between the populations (Caucasians and Afro-Americans and South Asians) they divided the waist circumference by the BMI. The waist/BMI ratio was significantly higher for Indian Men and Women, compared with all US races/sex groups. Results of these studies and that of many others have demonstrated that the South Asian population has excess visceral fat deposits, relative to overall body distribution [17]. If visceral fat is the "bad guy" then the million-dollar question is, does people undergoing liposuction get the benefit of losing this bad fat? If they do get benefit, then how long will it last? BMI is the most frequently used index of obesity; however, recent studies have shown that the body composition, than the size, may be more relevant risk factor [18]. Studies on Native Americans by Gray et al. have reported that obesity had a modest influence on risk factors for coronary artery disease, and that waist circumference had no special effect over BMI, on risk factors. They concluded, that American Indians might differ in many ways, including lifestyles and body composition; they may also differ widely in obesity and associated risks [19].

Endothelial Function and CMDs

Pathogenesis of atherosclerosis and associated vasculo-pathies begins in childhood and it is accelerated, with increase in body weight. Endothelium the largest organ system of the body, which lines all the blood vessels, plays a very important role in the vessel wall physiology and function. To a large extent, the vessel wall compliance and the flow of blood are modulated by a fine balanced production of the vasodilators and vasoconstrictors. Altered state of the vascular endothelium known as endothelial dysfunction, is the earliest clinically detectable stage of the cardiovascular disease. Known risk factors such as high cholesterol, high blood pressure, smoking, aging, chronic infection and inflammation can all disrupt normal physiology and function of the endothelium and lead to endothelial dysfunction. Aaron Kelly and associates in St. Paul Heart Clinic, St. Paul, Minnesota, followed a group of overweight children with known endothelial dysfunctions, as they participated in four-times-weekly exercise sessions on a stationary bike. After just eight weeks, the exercise group demonstrated dramatic systemic improvement in vascular health, with endothelial functions returning to normal [20-23]. The study participants did not lose weight nor reduce the body fat. This clearly demonstrates that if kids get to exercise early enough, regardless of being overweight, can have a chance at healthy life. In a separate study, Hambrecht and associates showed that exercise training improves endothelium dependent vasodilatation both in epicardial coronary vessels as well as in resistance vessels, in patients with coronary artery disease [24,25].

Mechanisms Underlying Diabetes-related Clinical Complications

By and large, the major goals in caring for patients with diabetes are to prevent, or at least slow, the development of clinical complications such as: Micro-vascular (eye and kidney disease), accomplished though control of blood sugar and blood pressure; Macro-vascular (coronary, cerebro-vascular, peripheral vascular), through control of lipids, hypertension and smoking. However, we do not know how the elevated levels of blood glucose, circulating insulin, and altered blood pressure modulate the physio-pathology of the blood vessels and induce severe dysfunction of this system. For instance, obesity has been associated with type-2 diabetes for several decades. The major basis for this link is the ability of obesity related altered lipid metabolism and its relationship with observed insulin resistance. Insulin resistance is linked with a variety of disorders such as hypertension, hyperlipidemia, atherosclerosis and metabolic syndrome. According to some recent studies, obesity may be a proxy than the cause, for insulin resistance. In the USA alone, there are 30 million individuals, who are obese with no insulin resistance. On the other hand, there are 6 million lean people, who have insulin resistance. Little is known about how the epigenetic factors such as the food that we eat modulates gene expression, in terms of proteomic and metabolomics. These are very important problems. However, future scientific studies could provide answers to such complicated questions.

Therefore, in the absence of such a knowledge base, the current strategies revolve around management of known risks. If we need to manage this chronic disease better, it is essential to understand the genomic, proteomic and metabolomic alterations that predispose the individuals, to develop these cardio-metabolic disorders. It is also important to understand the various gene expressions, mutations and polymorphisms that modulate the clinical complications of this chronic metabolic disease. If we can find gene expressions that modulate the risk associated with various clinical complications and associated earlier
thus is a main problem resulting from glucose toxicity. It is also supposed that in situations has ill effects on vessel wall physiology and function as well as for other individual risk factors. Major risk factor intervention trial (MRFIT) demonstrated the benefits of multiple risk factor control (www. trialresultscenter.org/study/7914-MRFIT.htm). It was a randomized study of over 12,800 subjects grouped according to either special intervention, stepped up care for hypertension or counseling for cigarette smoking.

Platelet Hyper-function and Clinical Complications

So far we have discussed some of the known risk factors for T2D, such as hyperglycemia, insulin resistance, obesity and metabolic syndrome. When it comes to managing such a complex disease, it is important to consider the not so common risks as well, so that a customized holistic treatment protocol can be developed. There is increasing evidence suggesting that the inflammatory mediators play a pathogenic role in the atherogenesis as well as in acute coronary syndromes [44-46]. Several recent studies suggest, that inflammatory cytokines such as tumor necrosis factor (TNFα), Interleukin (IL-1) and various chemokine (IL-8) may activate matrix metalloproteinase and induce degradation of connective tissue and promote apoptosis of cells in the atherosclerotic lesion, thus promoting plaques.
Management of Hyperglycemia, Diabetes and its Clinical Complications

Diabetes is a major public health problem of global importance. With the increase in age of the global population, incidence of this chronic complex disease is growing in alarming proportions. According to Dr Venkat Narayan of Center for Disease Control (CDC), Atlanta, Georgia, USA, diabetes is a common, growing, serious, costly and potentially preventable global public health problem [60]. In view of these observations, a multidisciplinary team of health professionals should provide diabetes care with expertise in diabetes management, working in collaboration with the patient and family. However this is not the way it is done in majority of countries. The current treatment strategies revolve around management of known risks. By and large, the major goals in caring for patients with diabetes are to prevent, or at least slow, the development of clinical complications, Diabetes is a serious disorder mainly due to its clinical complications. Control of postprandial hyperglycemia by intensive insulin therapy is fundamental to prevention of diabetes related clinical complications [26]. Having said that, the question is, can we accomplish such a tight control of postprandial glucose (2hPPG), by other treatment modalities? This approach of tight control of 2hPPG also seems to be useful in including the pre-diabetics into the prevention program. In view of this prevention strategy, it should be of great interest for the developing world, to evaluate and develop alternate therapies using indigenous and traditional medicine. Using Indian or Chinese Traditional Knowledge Systems, it is possible to bridge the current innovation deficit and open entirely new avenues of research and practices to facilitate a better healthcare.

Integrated Approach to the Management of CMDs

Integrative medicine is an approach to health care, which can be easily incorporated by all medical specialties and professional disciplines including Indian and Chinese Traditional Health Systems and all other health care systems worldwide [61]. Although traditional therapies are well accepted in India and neighboring countries including China, European Union and USA have not approved these therapies. In recognition of the growing body of evidence in support of Traditional or Alternate Medicine, in February of 2009, Institute of Medicine (IOM) of NIH, USA, organized a summit on Integrative Medicine. The IOM summit summary states, "The disease driven approach to healthcare has resulted in spiraling costs. The first priority for any health care system using and integrative approach is, to ensure that the full spectrum of preventive opportunities–clinical, behavioral, social, spiritual and environmental are included in the care and delivery process". Over 50 US Academic Institutions have Complementary and Alternate Medicine (CAM) programs funded by the National Center for Complimentary and Alternate Medicine (NCCAM). Therapeutic aspects of Traditional Medicine in which herbal products or herbal preparations are used have no place in this system. According to Dr. Josephine Briggs the Director of NCCAM/NIH, the evidence base for these approaches using modern rigorous methods of randomized trials is quite thin. However, according to a recent report in New York Times article dated April 22, 2014, titled, “A top Hospital Opens Up to Chinese Herbs as Medicines’, Cleveland Clinic, one of the country’s top hospitals, has opened up an “herbal clinic”. In addition, Northwestern University and North Shore University Health System affiliated to University of Chicago, both include herbal medicine among other treatment modalities offered.

Professor Bhushan Patwardhan, a well-known scientist of great
repute, from Pune, India, suggests, that with the help of Indian Traditional Knowledge systems, it is possible to bridge the current innovation deficit and open entirely new avenues of research and practices to facilitate a "rebirth of health care" in countries like India and China, who have ancient arts of traditional healing systems [61].

Till such a novel new approach is developed to bridge the inequities in current healthcare, we will have to consider what other known observation-based or evidence-based remedies are available for better management of diabetes related risk factors. Considering the large number of children born with low birth weight, we need to develop an appropriate nutritional supplement that will provide daily minimum requirement for would be mothers and growing child, to prevent intrauterine complications induced by insufficient nutrition. In the absence of an "all inclusive" healthy diet, it seems that a diet similar to Mediterranean-style diet, including a lower calorie content of refined carbohydrates, high content of fiber, moderate content of fat (preferably unsaturated) and moderate to high content of vegetable proteins are recommended [62,63]. Studies also have shown that insulin resistance and endothelial function are improved after folate and Vitamin B12 therapy, in patients with metabolic syndrome [64]. Omega-3 fatty acids supplements have been shown to improve the cardiovascular risk profile of subjects with MS, including markers of inflammation and auto-immunity [65]. Acetyl-L-carnitine has been shown to ameliorate hypertension and insulin resistance in subjects with increased risk for CVD [66].

We at the IPC Heart Care, Mumbai, India (www.ipcheartcenter.com) are evaluating, green tea of mulberry as well as green tea from regular tea leaves as supplements to manage postprandial hyperglycemia. A major green tea polyphenol, epigallocatechin-3-gallate, inhibits obesity, metabolic syndrome and fatty liver in high-fat-fed mice model [67]. In addition to the tea mentioned above, we also are evaluating D-ribose, L-arginine, Curcumin, Carnitine, Reveratrol, Anthocyanin-rich blueberry extract, citrus-derived flavonoid Narangenin, grape seed extract Procyanidon, green tea extract Teagreen, mulberry leaf extract 1-deoxynojirimicin (DNJ), water soluble extract of cinnamon and coffee (Green Coffee), and hibiscus tea. Based on the results of our studies, we plan to develop a "poly-pill" with indigenous phyto-chemicals for the management of postprandial hyperglycemia. Since we use TM-Oxi system (LD-Technologies, Miami Florida) to monitor risk profile of patients, we can evaluate various indigenous therapies for their effectiveness or otherwise, in managing the observed risks of MS, T2D and CVDs, using this non-invasive diagnostic platform.

Emerging Technologies: Early Detection and Management of CMDs

There is a great need for the development of a non-invasive comprehensive diagnostic platform, for early detection of cardio-metabolic disorders such as, hypertension, central abdominal obesity, metabolic syndrome, Type-2 diabetes, various vasculopathies, heart disease and stroke. Several studies have demonstrated the usefulness of monitoring health of the blood vessels by using techniques that measure, Intima-Media Thickness (IMT), Pulse Wave Velocity (PWV), Ankle-Brachial Index (ABI), Carotid Duplex Ultrasound (CDU) Index, and Vessel Wall Plaque Volume (3D Carotid Ultrasound). Although many methodologies are available for early detection of altered vascular function, the most widely used method is monitoring aortic Pulse Wave (PWV). With the advance in technologies, now it is possible to use multiple technologies and build a comprehensive risk assessment platform. It is also possible to add capabilities for risk prediction in such a platform. Availability of such a diagnostic platform will facilitate the surveillance of cardio-metabolic disorders at the community level. To accomplish our goals, we need a multi-functional diagnostic platform. Therefore, we have approached Bio Medical Electronics Group of BMS Engineering College, Bangalore, as well as National Design Research Forum (NDRF), Bangalore, India, to help us develop such a medical device development platform. Genesis Medical Systems, Hyderabad, India, is working for several years on the development of non-invasive Point-Of-Care devices for cardiovascular applications. Since they already have several non-invasive devices for monitoring vascular function, they can develop a comprehensive Cardio-Metabolic Risk Profiler (CMRP), to meet our requirements. We are collaborating with them not only in the development of CMRP but also in the validation studies of their all-in-one device under development, at our clinic in Mumbai (IPC Heart Care Clinic) and in California.

In the meantime, we are looking at the available POC devices worldwide, which can be used for early detection of cardio-metabolic disorders such as hypertension, glucose intolerance, type-2 diabetes and its clinical complications. LD Technologies of Miami, Florida (www.ldtech.com) specializes in the development of non-invasive Point-Of-Care devices. They have put together a platform called "RISC", (for Life Span, India), which uses Autonomic Nervous System (ANS) tests, Heart Rate Variation (HRV) tests, SudoMotor Function tests, and The TM-Oxi system. The diagnostic platform used at the IPC Heart Care (TM-Oxi), Mumbai and the Life Span Kiosk (RISC) in different cities in India, is a combination of many devices and uses photoplethysmography, spectrophotometry, oscillography and galvanic skin response technologies and displays data rapidly. The scores for various functional tests are color-coded (green orange, yellow and red) and printed out graphically as well as digitally. It generates impressive diagnostic reports with some recommendations. What we need today is a combination of these POC methodologies, for early detection of the altered physiology and function of blood vessels. In addition to these POCs, we should develop the ability to integrate other observed risk factors, to the data collected from such devices, to improve the risk score, so that one could use such comprehensive approach, to the early detection of vascular dysfunction, follow the progression and regression of the vascular disease and manage these diseases effectively.

Gene Therapy: Management of Diabetes Related Clinical Complications

Gene therapy is a method to replace mutated or diseased gene with a normal gene. Gene therapy based treatment provides long-term and sustained expression of the targeted gene. In gene therapy, gene of interest is packaged inside a carrier molecule. This carrier can be an engineered virus, liposome, arginine-grafted cyclaminobisacylamide-diaminohexane polymer (ABB) or a nano-complex. Non-viral methods can present certain advantages over viral methods, such as large-scale production and almost no host immunogenicity. Numerous non-viral gene delivery methods are under development for Glucagon-Like Peptide (GLP1) gene delivery. Oh et al. [68] reported that a single intravenous injection of Polylethenimine (PEI)/pGLP1 complex comprising a modified GLP CDNA in Zucker Diabetic Fatty (ZDF) rats resulted in an increase in glucose-induced insulin secretion with a reduction in blood glucose level for 2 weeks. Jean et al. reported a significant increase in the amount of plasma GLP-1 after chitosan-GLP-1 nanoparticles injection in ZDF rats [69]. This method improved glucose tolerance and reduced weight gain in the treated rats, but the increase in circulating insulin was transient. Non-viral gene therapy methods are safer; however, this drug delivery approach provides only transient effects [68,70].
Viral vectors are currently the best choice for gene transfer. There are various virus vectors that are being used for human gene therapy such as retrovirus, lentivirus, adenovirus and Adeno-Associated Virus (AAV). Among the viral vector tested, retroviral vectors have the ability to transform the single stranded RNA genome into a double stranded DNA molecule that stably integrates into the target cell genome. Recently, retroviral vector-mediated gene transfer has been re-invigorated with the development of lentiviruses. Lentiviral infection has several advantages including high-efficiency infection of dividing and non-dividing cells; integration property of lentivirus into the host cell genome provides long-term stable expression of a transgene, and low immunogenicity [71]. However, there are many concerns such as, possible generation of replication competent lentivirus during vector production and insertional mutagenesis leading to cancer [72]. All these safety concerns limit the use of retro and lentivirus in human gene therapy.

Adenoviral vectors are very efficient in transducing a wide range of tissues and offer an ability to infect both dividing and non-dividing cells, to produce high titer yield and accommodate large transgenes [73]. However, adenovirus elicits severe immune response, which limits the longevity of transgene expression [74]. Similar to adenovirus vectors, AAV-based vectors can infect both dividing and non-dividing cells. These vectors elicit only minimal immune response and hence are safer to use in human gene therapy studies. However, there are certain limitations of AAV vectors such as their reduced transduction efficiency and limited transgene capacity [75,76]. To increase the transduction efficiency researchers developed double-stranded (ds) AAV vectors by generating mutations at the ITR resulting in the preferential packaging of double-stranded, hairpin-like DNA dimers into AAV capsids [77]. Researchers are continuously modifying traditional AAV based gene therapy approach to make it more feasible for type 2 diabetes treatment.

Riedel et al. used DsAAV8-MIP construct with GLP-1 to assess therapeutic efficacy of GLP-1 via intra-peritoneal injection into diabetic mice. This approach provided protection from hyperglycemia in infected mice [78]. In another study aAV vector-mediated delivery of GLP-1 and N and K1 domains of human growth factor (HGF) delayed diabetes onset in db/db mice inducing pancreatic islet cell proliferation [79]. Recently, AAV5 mediated Exendin-4 delivery into the salivary glands resulted in sustained Exendin-4 expression at pharmacological levels in blood and salivary glands of diabetic animals [80]. This approach leads to improved glycemic control and insulin sensitivity associated with weight loss [81,82]. Although, some obstacles remain to be overcome, the risk-benefit ratio of gene therapy for type 2 diabetes treatments provide better alternative than life long disease management and diet regulation.

Conclusions

In conclusion, diabetes is a chronic, complex, fast growing disorder worldwide and is potentially preventable. This disorder is serious because of its clinical complications. As evidenced by major clinical trials in the USA and UK, tight control of hyperglycemia, prevents or reduces diabetes-related clinical complications such as retinopathy, neuropathy, nephropathy, skin infections and foot ulcers. Both India and China are racing rapidly towards claiming the title, “Diabetes Capital of the World”. Diabetes health care burden will be serious in developing countries as well as in resource poor countries of the world. Development of affordable multi-functional diagnostic platforms, will facilitate the detection of various risk factors at the earliest stages of this disease, as well as help us follow the progression and regression of the disease. Effective, integrated management of the known risks will slow/reduce or prevent diabetes related clinical complications. Both India and China have well-established Traditional Medical Systems, and therefore with the holistic approach, it is possible to develop new and novel approaches to the management of this complex metabolic disorder. A better understanding of the underlying causes that promote various clinical complications of diabetes and developing novel ways to manage the postprandial glucose peaks will reduce the health care cost considerably.

References


