

## Management of Diabetes Epidemic: Global Perspective

**Gundu HR Rao\***

*Emeritus Professor, Laboratory Medicine and Pathology, Director, Thrombosis Research, Lillehei Heart Institute, University of Minnesota, USA*

**\*Corresponding Author:** Gundu HR Rao, Emeritus Professor, Laboratory Medicine and Pathology, Director, Thrombosis Research, Lillehei Heart Institute, University of Minnesota, USA.

**Received:** June 20, 2018; **Published:** June 29, 2018

### Abstract

Eight million largely preventable deaths from treatable diseases, costed \$6 trillion in lost economic welfare in low-and middle-income countries in 2015. If current conditions persist, low-and middle-income countries could lose collectively \$11 trillion in gross domestic product, by 2030 (Harvard Gazette, June 2018, June issue of Health Affairs). The analysis is based on the findings from the Global Burden of Disease (2015) Project, including estimates of morbidity and mortality of 38 diseases that are survivable in well-resourced health care settings, and calculations of the number of deaths across 195 countries, that could be prevented, if that same standard of care were available everywhere. The American Heart Association developed methodology to project future costs of care for hypertension, coronary artery disease (CAD), heart failure, stroke, and all other related causes from 2010 to 2030. This methodology avoided double counting of costs, for patients with multiple cardiovascular conditions. By 2030, 40.5% of the adult US population is projected to have some form of CAD. Between 2010 and 2030, real (208 billion) total direct medical cost of CAD management, are projected to triple from 273 billion to 818 billion. According to Margaret Chan, the Director-General of World Health Organization (WHO), Member States of WHO, have set an ambitious target to reduce premature mortality from non-communicable diseases (NCDs)-including diabetes-by one third; achieve universal health coverage; and provide access to affordable essential medicine-to all by 2030. In her address in the first WHO Global Report on diabetes, she continues to say, "We have enormous task at hand, which is why I welcome the publication of the first report [1]. The report makes an important contribution to our understanding of diabetes and its consequences". Incidence of type-2 diabetes has increased in the last two decades by four-fold. The Non-communicable Disease (NCD) Risk Factor Collaboration Group (NCD-Risk), in their seminal article in *The Lancet* (April 2016) concluded that, "if the post-2000 trends continue in the incidence and rise of type-2 diabetes, the probability of meeting the global target of halting or reducing the rise in the prevalence of type-2 diabetes by 2025 to 2020 levels worldwide, is lower than one percent" [2,3]. If the expert group like NCD Risk Factor Collaboration has no hope, how can one rely on the ambitious target of the participating nations of WHO, and their commitment to such healthcare policies. If you carefully look at the national level programs for reducing, reversing or prevention of type-2 diabetes epidemic in countries like China and India, it becomes evident that there is no way, we will see such drastic reduction in the incidence of excess weight, obesity, and type-2 diabetes in the near future [4]. Since the lifestyle diseases like excess weight, obesity, and metabolic syndrome contribute significantly to the increase in type-2 diabetes, they are not discussed separately under this theme [5-12]. In this overview, we will briefly discuss the diabetic "tsunami" from a global perspective, to create awareness in the scientific community, so that researchers, clinicians, healthcare workers, and policy makers, take this twin epidemic (obesity and diabetes) seriously, and develop novel strategies to reduce the healthcare burden from these metabolic diseases, of great public health interest.

**Keywords:** *Diabetes Epidemic; Global Perspective*

In the late 80s, when these metabolic diseases had just started to increase in their incidence, we at the University of Minnesota, led a delegation of experts to the WHO, Geneva, Switzerland and to present our case on the prevention of cardiometabolic diseases. As the team leader, and principle investigator, from the Lillehei Heart Institute, University of Minnesota (U of M), I had developed a proposal titled, "Reduction, reversal, and prevention of the fetal origin of adult diseases". We had in our delegation, one neonatologist (U of M), a biochemist (University of Winnipeg, Canada), a cardio-thoracic surgeon (Bengaluru, India), and a WHO consultant (UK). We met, the then Director General of WHO, Dr. Margaret Chan, NCD Chief, Dr. Shanthi Mendis, and other key players. In brief, we presented a case for early detection (intrauterine) of cardiometabolic diseases and development of a robust intervention and management strategy for the known risk factors. According to a National Institutes of Health (NIH, USA) summary, the main basis of the Barker hypothesis is, "that under nutrition in pregnancy impairs fetal growth, or promotes disproportionate fetal growth, and as a trade-off these adaptations that promote survival in adverse conditions, lead to limited physiological functions and development of adult diseases of fetal origin" [13-15].

Based on the results of seminal epidemiological studies done at the CSI Holdsworth Memorial Hospital (HMH), Mysore, in India, thirty percent of the children born (close to 800,000) are of low birth weight. The birth record of all the children born in this hospital is maintained from 1936 to the present time [7]. In view of this meticulous record keeping, Medical Research Council (MRC) of UK, has set up an epidemiology unit at this hospital. Studies from this group, from the researchers of the diabetes clinic, KEM, Hospital, Pune, and the researchers of the Indian Council of Medical Research (ICMR) for decades, have established that these low birth weight children as they grow to adulthood, have a higher incidence of metabolic diseases such as hypertension, obesity, metabolic syndrome, and type-2 diabetes. Our presentation received just a verbal commendation, and nothing came out of this effort. Well, what did we have in mind as possible intervention strategy? Our idea was to develop a comprehensive awareness, and educational program for the would-be parents, about the important role of micronutrients in reduction or prevention of low-birth weight children. In addition, we were planning to develop a sustainable low-cost micronutrient supplement for the would-be mothers. According to a study done in 2010 by the researchers of Harvard School of Public Health, every year more than 20 million infant are born with low birth weight worldwide [16]. More than one third deaths of malnourished children occur in Southern Asia and Sub Saharan Africa and this condition is attributed to maternal and child undernutrition. The authors conclude, "that maternal micronutrient supplementation increases birth weight of children, pregnant women who receive micronutrient supplement were less likely to deliver low-birth-weight infants". We had this type of a project in mind, when we presented our proposal to the WHO in the 90s and even after three decades, we do not see any such national level preventive programs in place, in the low and middle-income countries.

This problem is not unique to India, it really is a global problem, related to malnutrition [13,14]. China also faces similar problems, when it comes to the maternal and neonatal nutrition. In spite of the fact that we know of this risk for over 7 decades, no country has taken this problem as a serious public health burden. No country has established any interventions for reducing, reversing, or prevention of this known risk factor: Even in advance countries like the USA, according to some experts, guidelines regarding the optimal pregnancy, nutrition and weight gain, management of low-birth and high-fetal-weight pregnancies, use of maternal glucocorticoids, and new born feeding strategies, have yet to be fully integrated [15]. We in Asia, are adding millions of at "risk population", because of our indifference to develop better preventive healthcare policies. Now you can think about why no country has reduced, reversed or prevented the increase in the rise, or the prevalence of excess weight, obesity and type-2 diabetes. These are lifestyle diseases and hard to convince people to change their inherited or acquired habits. As the Harvard study has shown, these risks are preventable [16].

When we talk about early detection and management of risk factors, neonatal and maternal nutrition comes as one of the top priorities. On the other hand, Swedish researchers involving over 62,000 Danish individuals have demonstrated that childhood overweight is associated with an increased risk for developing type-2 diabetes in adulthood [17]. According to Minnesota researchers, in children, oxidative stress and adipokine levels, worsen throughout the continuum of obesity. Kelly and associates in Minnesota, conducted a study to assess subclinical inflammation, fasting insulin, and endothelial dysfunction, before and after exercise in overweight children. They

found in these children, inflammatory marker c-reactive protein was an independent component, compared with fasting insulin. Just eight weeks of exercise, improved fitness, HDL-cholesterol and endothelial dysfunction in this group [18]. A collaborative study between the staff of the University of Minnesota and Madras Diabetes Research Foundation(MDRF), Chennai, India, concluded that compared to the US, waist-hip ratio is significantly higher in men and women from India. These results support the hypothesis that South Asians are particularly predisposed towards central abdominal adiposity [19]. These and other studies facilitated the diagnosis of metabolic syndrome by using simple measurements of waist circumference and triglyceride levels. A recent study, based on the data from the National Health and Nutrition Examination Surveys (NHANES) between 1980 to 2014, examined the cardiovascular and renal burdens in adults with prediabetes over time and found that renal risks and vascular disease have become highly prevalent in adults with prediabetes [20].

According to a recent report by the Centre for Disease Control(CDC) and Prevention, 50% of the adults in the USA are prediabetic (84 million). It is a well-known factor, that the individuals with diabetes have a several fold higher risks for developing vascular disease. In view of these observations, it is reasonable to conclude, that worldwide increase in these twin epidemics, obesity and diabetes will contribute significantly, to the increased vascular disease including CVD. According to all estimates, cardiovascular disease is the number one cause for all-cause mortality worldwide. Can we then include cardiovascular disease also as an epidemic? In 2014 there was a debate in the Legislative assembly of Manitoba, Canada, about the “tsunami” of diabetes [21]. The members were concerned about the increasing healthcare cost, if the twin epidemic of obesity and diabetes were not controlled. All of the individual risk factors of CMDs pose as “tsunami” and collectively pose great challenge worldwide. This is not just an isolated case of diabetes epidemic, but shows the severity of the possible healthcare burden, which translates into economic disaster in many of the developing nations.

At the molecular level, emerging technologies like high-throughput profiling of metabolic status can be utilized to determine the risk of developing diabetes. Studies by the Harvard researchers and the Framingham heart researchers, have shown that five branched chain and aromatic amino acids, have highly-significant associations with future diabetes: isoleucine, leucine, valine, tyrosine, and phenylalanine [22]. A combination of three amino acids, predicted future diabetes (five-fold higher). These results underscore, the importance of amino acid metabolism early, in the pathogenesis of diabetes. Similarly, studies by Dr. Robert Freishtat and associates, at the Children’s National Memorial Hospital (CNMH) Washington DC, have shown that adipocyte-derived exosomes contain mediators (micro RNAs) capable of activating end-organ inflammatory and fibrotic signalling pathways [23]. Considering the role such a molecular mechanism may play in the fetal origin of adult diseases, we have facilitated a bilateral study between the researchers of CNMH and clinicians of Diabetes Group at the KEM Hospital, Pune, India. Although we advocate early screening for the detection of at risk individuals, at population level, it poses a huge economic challenge. Having said that, we would like to refer the readers to a study, on metabolic profiles of young-onset type-2 diabetes in South Asians; from Hong Kong (15,431), India (9107), Philippines (7712), China (5646), South Korea (1751), Vietnam (705), Singapore (385), Thailand (275), and Taiwan (107). One in five had young-onset diabetes. The authors concluded that, “in view of the risk conferred by the long-term suboptimum metabolic control, findings of this study suggest an impending epidemic of young-onset diabetic complications” [24].

China National HBA<sub>1c</sub> Surveillance System (CNHSS), did a cross sectional study on 222,773 Chinese patients with type-2 diabetes, in 630 hospitals from 106 cities in 30 provinces in 2012. Study concluded, “that patients with early-onset diabetes, had an increased risk for non-fatal cardiovascular disease, mostly attributable to longer duration of diabetes” [25]. Dr Anoop Shah and associates in UK, conducted a cohort study to determine the incidence of CVD in young adults of 30 years and old. They analysed the data from the CALIBER program which links data from four electronic health data sources [26]. The cohort had a total of 1.9 million individuals, 98.2% did not have diabetes and 1.8% (34,198) had type 2 diabetes. Of the diabetic population, 18% had a first CVD presentation, which was peripheral arterial disease; 16% had heart failure. In this study, the peripheral artery disease and heart failure were the most common initial manifestations of CVD -related complications. The authors suggest that new clinical trials on diabetes should now consider including peripheral artery disease as part of any composite CVD outcome.

Diabetes-related clinical complications include, retinopathy, nephropathy, neuropathy and vasculopathy. Heart attack and stroke are 2 to 4 times more common in diabetic subjects than non-diabetics. High blood pressure affects 2 out of three individuals with diabetes. Diabetes is the leading cause of blindness due to retinopathy and glaucoma. Diabetes is also the leading cause for end-stage renal disease. Approximately half of all people with diabetes have some form of nerve damage. The nerve damage is the major contributor for lower-extremity amputations. Majority of people who have diabetes are currently monitored with fasting glucose, post prandial glucose, or at the most with HbA<sub>1c</sub> levels. There is considerable interest in developing molecules (biomarkers) that help in the early diagnosis of progression and/or diagnosis of diabetic complications. Matheson, *et al.* have reviewed urinary biomarkers that may be used to monitor the progression of diabetes complications. Their conclusion was that biomarkers of renal dysfunction such as transferrin, type1V collagen, and N-acetyl  $\beta$ -D glycosaminidase may be more sensitive than the currently used marker microalbumin. In addition, inflammatory markers including orosomucoid, tumor necrosis factor- $\beta$ , transforming growth factor, and monocyte chemoattractant protein-1, as well as oxidative stress marker 8-hydroxy-2 deoxy guanosine, have been suggested as useful biomarkers [27]. The author concludes that, "In spite of the findings of the researchers and even the commendations in the guidelines, there is still a gap between the levels of target values of biomarkers to reduce the clinical complications, and the levels of these targets that could be achieved in actual medical practice". Researchers from Egypt have shown, that circulating miRNA-130 may serve as a potential biomarker for the identification of diabetics at risk for developing diabetic nephropathy [28]. Elevated levels of inflammatory cytokines, TNF -alpha, IL-6, leptins, leptin-adiponectin ratios, fibrotic markers, IGF $\beta$ P7 and TGF- $\beta$  seem to serve as biomarkers of diabetic cardiomyopathy [29]. Precision medicine seems to be the order of the day, promising optimum management of the metabolic disease, with the wealth of "Omics" data (genomic, metabolic, proteomic, environmental, clinical and preclinical) [30]. Molecular markers that can predict the probability of developing diabetes at a future date, or those which predict the early progress of the disease towards one of the many clinical complications of diabetes are worth exploring, as they provide us opportunity to reduce, reverse or prevent such developments.

### Management of Diabetes

In a short overview like this, it is rather difficult to cover all aspects of diabetes management. Hence, we will discuss few salient features of standard diabetes care, and preventive strategies at the population level. Clinicians worldwide diagnose and manage type-2 diabetes by monitoring fasting blood glucose (FBG), postprandial glucose (PPG), or glycated hemoglobin (HbA<sub>1c</sub>). As we have mentioned earlier, it is not feasible to screen prediabetes in the entire Indian or Chinese population or to systematically identify high risk groups by blood glucose tests, considering the huge populations in these countries. Other than a few industrialized nations, the situation is no different in majority of the resource poor countries. In view of this situation, prediabetic population worldwide, are left undiagnosed and as such, do not come under clinical management. Professional organizations, such as American Diabetes Association (ADA), American Heart Association (AHA), American Association of Clinical Endocrinologists (AACE), and American College of Physicians (ACP) have issued guidelines and guidance statements. With over 152,000 members, ACP is the largest medical speciality organization. According to Dr. Amir Qaseem, vice president for clinical policy at the ACP, "the organization created the new guidance statements, to help its members sort through conflicting HbA<sub>1c</sub> targets, advised by different professional groups". Since this is one of the latest guidance statements, we have reproduced verbatim the four guidance statements as a reference for our readers [31].

1). Clinicians should create personalized goals for glycaemic control in patients with type-2 diabetes. These goals should be based on clinician-patient discussion of benefits and harms of pharmacotherapy, patient preferences, the patient's general health and life expectancy, treatment burden, and costs of care. 2). Clinicians should aim to help their patients with type-2 diabetes achieve an HbA<sub>1c</sub> level between 7% and 8%. 3). If a patient with type-2 diabetes achieves an HbA<sub>1c</sub> level < 6.5%, clinicians should consider de-intensifying pharmacologic therapy. 4). In treating patients with type-2 diabetes, clinicians should aim to minimize symptoms related to hyperglycaemia. Clinicians should avoid targeting a specific HbA<sub>1c</sub> level in patients with a life expectancy of <10 years due to advanced age (80 or older); residence in a nursing home; or chronic conditions such as dementia, cancer, end-stage kidney disease, severe chronic obstructive pulmonary disease,

or congestive heart failure because, the harms outweigh the benefits in these patients. Soon after this guidance statement was published, the ADA and AACE, along with the American Association of Diabetes Educators and the Endocrine Society, expressed their disagreement with the recommendation. All of them said, that they “strongly disagree” with the higher targets suggested in the ACP guidelines (between 7 and 8). Guidelines are issued on the basis of the collective knowledge available. Having said, that it is up to the clinicians as to what should be the optimal HBA<sub>1c</sub> for his/her patient. Experts agree that the best HbA<sub>1c</sub> target for a patient with diabetes is a personalized one. Moreover, as we will discuss later in the article, HBA<sub>1c</sub> is just one of the parameters, and the management of diabetes has to be customized for each patient depending upon the medical history. Ultimate goal is not just lowering HBA<sub>1c</sub> but to reduce, reverse or prevent clinical complications associated with the progress of diabetes.

Now that we have briefly discussed the management of diabetes at the individual’s level, we will now discuss what is happening at the population level and examine some diabetes management strategies in various countries. I urge readers to refer the guidelines issued by the various professional societies to get an idea of what is the standard of care for diabetes management. Let us briefly consider the recommendations in Manitoba, Canada, with a population of just 1.3 million individuals. I have listed here the seven-point program that Dr. Jon Gerrard, a member of the legislative assembly (MLA) of Manitoba has recommended in his 2014 legislative report: 1) Develop an effective central leadership structure to address the epidemic – including strategic central information and innovation strategies. 2) Immediately implement current best practices for preventing diabetes province-wide. 3) Initiate a vigorous effort combining pilot programs and research to improve prevention. 4) Fully review the critical issues that have not been tackled in the 1998 strategic plan that was proposed to address the diabetes epidemic. 5) Approach diabetes as a disease of nutrient deficiencies and not just nutrient excess. 6) Incorporate recent findings involving the hepatic insulin sensitizing substance and other advance in improving prevention of diabetes. 7) Develop and implement a comprehensive plan and budget to sufficiently address the epidemic.

Now let us see what the National Health Service (NHS) of UK is doing with a population close to 66 million: The NHS plans to develop, implement and monitor strategies to reduce the risk of developing Type-2 diabetes in the population as a whole, and to reduce the inequalities in the risk of developing Type-2 diabetes. The NHS will also develop, implement and monitor strategies to identify people who do not know they have diabetes. All children, young people, and adults with diabetes, will receive a service which encourages partnership in decision-making, supports them in managing their diabetes and helps them to adopt and maintain a healthy lifestyle. This will be reflected in an agreed and shared care plan, in an appropriate format and language. Where appropriate, parents and caregivers should be fully engaged in this process. All adults with diabetes will receive high-quality care throughout their lifetime, including support to optimize the control of their blood glucose, blood pressure, and other risk factors for developing the complications of diabetes. All children and young people with diabetes, will receive consistently high-quality care and they, with their families and others involved in their day-to-day care, will be supported to optimize the control of their blood glucose and their physical, psychological, intellectual, educational and social development.

Now let us look at the strategies in China with population exceeding 1.3 billion. In a country like China, where one finds a quarter of all diabetes cases in the world, the government and its partners are continuously trying to catch-up with this growing and costly epidemic. Looking from a global perspective, there exist tools, technologies, and the knowledge, to diagnose and effectively manage the disease. According to China’s own data, at least 580 million Chinese were estimated to have at least one modifiable NCD-related risk factor in 2010. Between 70 and 85 per cent of these people were under 65. To tackle the NCD challenge in 2012, China released the National Plan for NCD Prevention and Treatment (2012 - 2015), highlighting the importance of both primary prevention of NCDs through promoting healthy life styles, as well as secondary prevention through improving treatment and management of NCDs, especially in primary health care settings.

Professor Mange Han and associates from Fudan University, Shanghai, China, describe the evolution of NCD disease prevention and control in China the following way: “The 70-year experience of China, in fighting against non-communicable diseases (NCDs), can be classified into three distinct periods: 1) the disease-oriented strategy period (from 1950 to 1994); 2) the risk factor-focused strategy period

(from 1995 to 2008); and 3) the social and policy priority strategy period (since 2009). A number of projects were successful and valuable experience and lessons were accumulated during the three periods. Due to the underestimation of the 'explosive' epidemic of NCDs, however, it took China quite a long time to find the right path to curb the upward trend in these diseases. In view of the seven decades of China's experience, findings of this and other reports of similar nature, will have valuable implications for other low-and middle-income countries". (<https://doi.org/10.1177/1757975917739621>. 2017). With an estimate of 200 million additional people in the world with diabetes by 2035, it is clear, that we cannot "treat our way" out of the disease. Where there is a significant gap in quality of diabetes care in middle income countries (MICs) is, the on-the-ground implementation of programs, to reduce the incidences of diabetes-healthcare infrastructure. Improved infrastructure means, action from the national governments, in unilateral initiatives, as well as in partnership with other health organizations. National level commitment for combating these epidemics is lacking in many countries.

The goal of primary prevention is to prevent the occurrence of T2DM. Secondary prevention, aims to prevent diabetic complications in patients with T2DM. Tertiary prevention, aims to delay the progression of diabetic complications, to reduce morbidity and mortality, and to improve the patients' quality of life. These guidelines recommend, that patients with prediabetes lower the risk of diabetes through diet control and exercise; that patients should receive regular follow-up that provides psychosocial support to ensure patients' long-term adherence to a healthy lifestyle; that blood glucose levels should be regularly tested; that the cardiovascular disease risk factors (such as smoking, hypertension and dyslipidaemia) should be closely monitored; and that appropriate intervention measures should be provided. These guidelines recommend that for newly diagnosed diabetes patients and early T2DM patients, strict glycaemic control strategies should be adopted to reduce the risk of diabetic complications. Setting goals is different from achieving the goals. Undiagnosed, diabetes in China is associated with preventable complications and mortality as well as considerable costs. The current management of type 2 diabetes (T2D) in China, appears to be far from optimal-only 26% of patients receive consistent treatment, and of those, only 40% attain adequate glycaemic control. If this is the situation in China, after seven decades of experience and planning, imagine the state of affairs in less developed or resource poor countries.

Public awareness campaigns warning people about diabetes and its complications (heart disease, blindness, kidney failure, amputation), have failed even in an advanced country like the USA. The Centers for Disease Control(CDC) and Prevention, estimates that nearly a quarter of diabetics don't even know they have the disease. How about prevention? Excess weight and obesity are the underlying causes of late-onset Type-2 diabetes, which accounts for more than 90% of new cases. Today, about 40% of U.S. adults are considered obese, up from about 30% two decades ago, according to the latest CDC report. According to the latest issue of *Diabetes Care*, a journal of the American Diabetes Association, despite the introduction of 40 anti-diabetic drugs and drug combinations since 2005, including several long-acting versions of insulin, the proportion of diabetics achieving adequate blood-sugar control, remains stuck at about half. What's the federal government doing about any of this? Nothing we can see beyond public relations claptrap like, declaring National Diabetes Day/Month. I too attended one such meeting on the 14<sup>th</sup> of November in the City of Chennai, India. Situation is no different at the Global level, even with the Global Health Initiatives or Millennium Development Goals of the United Nations, or WHO Global Diabetes Care. If this is the true picture of Diabetes Care and Management at the Global level, think of pathetic situation in less developed countries and the resource poor countries?

A study of cardiometabolic diseases in 26 industrialized countries, reported a significant decline in the deaths due to cardiovascular disease [32]. The same study found, that diabetes-related deaths increased in these countries. We interpret this finding as indicative of the success in treating the modifiable risk factors for CVD effectively. Several studies have demonstrated that just managing effectively the modifiable risk factors will reduce the CVD deaths and significantly influence the outcome [35,36]. Having said that, it seems evident from the results of this comprehensive study, that the same is not true for diabetes management in these countries. Because, in a recent article in the *New England Journal of Medicine*, the authors reported that rates of all the five complications related to the progress of diabetes declined between 1990-2010 in the USA. Largest decline was noticed in acute MI, and death from hyperglycaemic crisis, followed by stroke, and amputations. Smallest decrease was in end-stage renal disease [34].

Diabetes is an important public health problem worldwide. Since 1980 the incidence of diabetes has increased by four-fold, from 108 million to 422 million in 2014. Effective approaches are available to prevent type-2 diabetes and its complications [24-34]. According to a WHO report (2014), these include, policies and practices across whole populations and within specific settings (school, home, workplace), that contribute to good health for everyone, regardless of whether they have diabetes, such as exercising regularly, eating healthy, avoiding smoking, and controlling blood pressure. Report further emphasizes, that no single policy or intervention can ensure this transition to a healthy society. It calls for a whole-of-Government and whole -of- society approach. Several clinical trials have demonstrated that management of modifiable risk factors by just healthy lifestyle, significantly reduces the development of acute vascular events [35,36].

The starting point for living well with diabetes is early diagnosis-the longer a person lives with undiagnosed and untreated diabetes, the worse their health outcomes are likely to be. Easy access to the basic diagnostics, such as blood glucose testing, should therefore be available in primary health-care settings. For those who are diagnosed with diabetes, a series of cost-effective interventions can improve outcomes, regardless of what type of diabetes they may have. These interventions include, blood glucose control, through a combination of diet, physical activity and medication; control of blood pressure and lipids to reduce CVD risks, and screening of damage to the eyes, nerves, kidneys, and feet. Diabetes management can be strengthened through the use of “standard protocols” and “standard of care” developed by professional societies like ADA, AHA, ACCE, ACP etc.

### Conclusions

All the metabolic risk factors associated with the development of type-2 diabetes and its clinical complications, such as excess weight, obesity, metabolic syndrome, and vascular diseases, have reached epidemic status worldwide [37-39]. We were pleasantly surprised that a State in Canada (Manitoba), with less than 1.3 million people, had extensive debate on the “diabetic tsunami”, and came up with a seven-point program, to contain this epidemic. We were equally surprised, about the indifference and lack of seriousness in developing countries like India, with a huge population of diabetics, where we see very little effort in diagnosing, monitoring, or management of such an epidemic. We have discussed early diagnosis of the risks for developing diabetes, such as intrauterine nutritional constraints, childhood obesity, excess weight, obesity, prevalence of prediabetes, and undiagnosed individuals. We also have discussed the need to develop exploratory research to identify biomarkers that indicate the future development of diabetes, as well as those specific miRNAs, elevation of which, would indicate the progress of the disease leading to various clinical complications such as retinopathy, nephropathy, neuropathy and vasculopathies. We have briefly described, the standards of care, as well as preventive strategies in Canada, UK, the USA and finally, some Global efforts. We feel a sense of loss, to see that for such a huge public health problem, which is described as “epidemic” or “tsunami”, there is no adequate uniform global response. Just coming up with resolutions, guidelines, guidance statements, may not be adequate to stop, or reduce, or prevent the incidence, or the rise of these chronic metabolic diseases.

We are talking about the rise in the incidence of diabetes from 108 million to 422 million in just two decades. But if we look at the other metabolic risks that contribute significantly to this increase, as well as to the increases in all cause deaths, associated with these chronic diseases, then you will understand the magnitude of this public health problem. Excess weight and obesity has been diagnosed in over 2.1 billion people worldwide, that is roughly 30% of the adult population of the world [37]. Hypertension is another major risk factor. Number of individuals with hypertension has been reported to have reached from 600 million (1980) to over a billion (2008) worldwide [38]. Similarly, another contributing risk factor, metabolic syndrome also has been on the rise. Currently, over a billion individuals suffer from metabolic syndrome worldwide [39]. Transition in the global economy, socio-economic disparities, work-related stress, lack of physical activity, altered diet, increased pollution, and many other epigenetic factors, have significantly contributed to this observed increase in the incidence of chronic metabolic diseases.

According to AHA, in the USA, between 2010 and 2030, real (208 billion) total direct medical cost of CAD management, are projected to triple from 273 billion to 818 billion. Just as an example of the impact of chronic metabolic disease burden on countries with huge population, let us compare India and China. With the world’s two largest populations, India and China are facing substantial health chal-

lenges. With India projected to overtake China in population by 2028, China serves as a useful guide for India's health and development trajectory. The total losses with physical disease and mental health for China are 18.5 trillion and 4.5 trillion. The estimated losses over the entire time period (2012 - 2030) roughly 4.5 trillion, equates more than six times India's total health expenditure over the previous 19 years. The estimated losses for China are more than ten times total health expenditure in the last 19 years prior to 2012 [40]. Time to act is now, not later or in the near future. If we fail to act now, it will be impossible to prevent the severe economic disaster in many countries, in which these twin epidemics will cause a havoc.

Finally, I would like to conclude this mini-review, with a summary statement from the World Bank, on this very important topic of public health interest. The World Bank after an international conference published their report in 2011 titled, "The Growing Danger of Non-Communicable Diseases: Acting Now to Reverse Course" [41]. In this report they say, that despite the magnitude of the challenge, there is considerable hope for action, especially if policy makers and communities mobilize broadly behind evidence, make prevention and targeted treatment of such diseases a priority. They continue, "the potential cost of NCDs to economies, health systems, households and individuals in middle-and lower-income countries is high". They further assure, "that they stand ready to help countries, particularly those dealing with a "double burden" of disease, to shape strategies to achieve their MDG targets". They conclude, "Worldwide, the best examples of measures to address NCDs show that such efforts can deliver health improvements sooner than commonly thought-within a few years of the elimination of exposure to risk factors, or even more quickly. Leaders at the national and local level have the power to save many lives, avoid widespread suffering, and forestall major human and economic cost, all within a short space of time. Now is the time to act".

### Bibliography

1. Global Report on Diabetes: 1. Diabetes Mellitus-epidemiology. 2. Diabetes Mellitus-prevention and control. 3. Diabetes, Gestational. 4.. Chronic Disease. 5.. Public Health. WHO. (NLM Classification: WK 810. (2016).
2. NCD Risk Factor Collaboration (NCD-Ris-C.: Worldwide trends in bod-mass index, underweight, overweight, and obesity from 1975-2016: a pooled analysis of 2416 population-based measurement studies in 128.9 million children, adolescent, and adults". *Lancet* 390.10113 (2017): 2627-2642.
3. NCD Risk Factor Collaboration. "Worldwide trends in diabetes since 1980: a pooled analysis of 751 population-based studies with 4.4 million participants". *Lancet* 387.10027 (2016): 1513-1530.
4. Mohan V and Rao GHR. "Type-2 diabetes in South Asians: Epidemiology, Risk Factors and Prevention". *Jaypee Medical Publishers New Delhi, India.* (2007).
5. Rao GHR., *et al.* "Clinical complications of Type-2 diabetes mellitus in South Asians and Chinese Populations: An Overview". *Journal of Diabetes and Metabolism* 5 (2014): 420.
6. Rao GHR. "Prevention or reversal of cardiometabolic diseases". *Journal of Clinical prevention Cardiology* 7.1 (2018): 22-28.
7. Rao GHR., *et al.* "First step for prevention of cardiometabolic disease". *Journal of Cardiology Photon Journal of Photon* 109 (2016): 179-186.
8. Rao GHR. "Interventions in Obesity and Diabetes: Point of view". *Interventions in Obesity and Diabetes* 1 (2017).
9. Rao GHR. Type-2 diabetes, a Global Epidemic. *Journal of Endocrinology and Thyroid Research* (2017): ID. 555552.
10. Rao GHR. "Importance of studying disease and disease process". *Developments in Clinical and Medical Pathology Crimson Publishing* 1 (2018) 1.

11. Rao GHR. "Novel sub-groups of adult-onset diabetes and its clinical complications". *Archives of Endocrinology and Diabetes* 1:1 (2018).
12. Rao GHR. "Coronary Artery Disease. MacMillan Med. Publ. (Nature/Spring, Springer Healthcare Education, New Delhi, India.
13. Barker DJP, *et al.* "Fetal Origin of adult disease: strength of effects and biological basis". *International Journal of Epidemiology* 31.6 (2002): 1235-1239.
14. Forsen T, *et al.* "The fetal and childhood growth of persons who develop type-2 diabetes". *Annals of Internal Medicine* 133.3 (2000): 176-182.
15. Lau C, *et al.* "Fetal programming of adult disease: implications for prenatal care". *Obstetrics and Gynecology* 117.4 (2011): 978-985.
16. Kawai K, *et al.* "Maternal multiple micronutrient supplementation and pregnancy outcomes in developing countries: meta-analysis and meta-regression". *Bull WHO* 89.6 (2010): 402-411B.
17. Bjerregaard LG, *et al.* "Change in overweight from childhood to early adulthood and risk for type-2 diabetes". *New England Journal of Medicine* 378 (2018): P1302-1312.
18. Kelly A, *et al.* "Inflammation, insulin resistance and endothelial dysfunction in overweight children and adolescents". *Journal of Pediatrics* 145.6 (2004): 731-736.
19. Bajaj H, *et al.* "Comparison of relative waist circumference between Asian Indian and US adults". *Journal of Obesity* (2014): 461956.
20. Ali M, *et al.* "Cardiovascular and renal burdens of prediabetes in the USA: analysis of data from serial cross-sectional surveys, 1988-2014". *Lancet Diabetes Endocrinology* 6.5 (2018): 392.403.
21. Jonathan M Gerrard. "The Diabetes Epidemic in Manitoba: It is not just sugar". Manitoba Liberal Caucus Report. Dr. Jon Gerrard, MLA-River Heights (2014).
22. Wang TJ, *et al.* "Metabolite profiles and the risk of developing diabetes". *Nature Medicine* 17.6.4 (2011): 448-453.
23. Ferrante SC, *et al.* "Adipocyte-derived exosomal miRNAs: A novel mechanisms for obesity-related disease". *Pediatric Research* 77.3 (2015): 447-454.
24. Huo X, *et al.* "Risk of non-fatal cardiovascular disease in early-onset versus late-onset type-2 diabetes in China: a cross-sectional study". *The Lancet Diabetes and Endocrinology* 4.2 (2016): 115-124.
25. Yeung RO, *et al.* "Metabolic profiles and treatment gaps in young-onset type-2 diabetes in Asia (the Jade Programme: a cross-sectional study of a prospective cohort". *The Lancet Diabetes and Endocrinology* 2.12 (2014): 935-943.
26. Shah AD, *et al.* "Type-2 diabetes and incidence of cardiovascular disease: a cohort study in 1.9 million people". *The Lancet Diabetes and Endocrinology* 3.2 (2015): 105-113.
27. Matheson A, *et al.* "Urinary biomarkers in type-2 diabetes: a review". *Diabetes/Metabolism Research and Reviews* 26.3 (2010): 150-171.
28. Motawi TK, *et al.* "Potential serum biomarker for early detection of diabetic nephropathy". *Diabetes Research and Clinical Practice* 136 (2018): 150-158.
29. Shaver A, *et al.* "Role of serum biomarkers in early detection of diabetic cardiomyopathy in the West Virginia population". *Journal of Medical Sciences* 13.3 (2016): 161-168.

30. Kraniotou C., *et al.* "Predictive biomarkers for type-2 diabetes mellitus: Bridging the gap between systems research and personalized medicine". *Journal of Proteomics* (2018).
31. Qaseem A., *et al.* "Hemoglobin A1c targets for glycemic control with pharmacologic therapy for nonpregnant adults with type 2 diabetes mellitus: a guidance statement updates from the American College of Physicians". *Annals of Internal Medicine* 168.8 (2018): 569-576.
32. Di Cesare M., *et al.* "The contributions of risk factor trends to cardiometabolic mortality decline in 26 industrialized countries". *International Journal of Epidemiology* 42.3 (2013): 838-848.
33. Weng J., *et al.* "Standards of care for type-2 diabetes in China". *Diabetes/metabolism Research and Reviews* 32.5 (2016): 442-458.
34. Gregg EW., *et al.* "Changes in diabetes-related complications in the United States 1990-2010". *New England Journal of Medicine* 370 (2014): 1514-1523.
35. Yusuf S., *et al.* "Effect of potentially modifiable risk factors associated with myocardial infarction in 52 countries (the INTERHEART study: Case-control study)". *Lancet* 364.9438 (2004): 937-952.
36. Khera AV., *et al.* "Genetic risk, adherence to a healthy lifestyle, and coronary artery disease". *New England Journal of Medicine* 375 (2016): 2349-2358.
37. Obesity Collaborators GBD. "Health effects of overweight and obesity in 195 countries over 25 years". *New England Journal of Medicine* 373 (2017): 13-27.
38. Mills KT., *et al.* "Global disparities of hypertension prevalence and control. A systematic analysis of population-based studies from 90 countries". *Central India Regional Council* 134 (2016): 441-450.
39. Saklayen MG. "The global epidemic of Metabolic Syndrome". *Current Hypertension Reports* 20 (2018): 12.
40. Economics of Non-communicable Disease in India. Harvard School of Public Health. Department of Global Health and Population. A report by the World Economic Forum and Harvard School of Public Health (2014).
41. The World Bank. "The Growing Danger of Non-Communicable Diseases: Acting Now to Reverse Course. Conference Edition. The World Bank, 1818 H Street, N.W. Washington DC 20433 (2011).

**Volume 3 Issue 2 July 2018**

**©All rights reserved by Gundu HR Rao.**