Convergence on the Constraints and Challenges in the Awareness, Prevention, Treatment and Control of Type 2 Diabetes and Diabetes-Related Conditions

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Abstract

The global epidemiology of type 2 diabetes over time regarding the biologic, cultural, demographic, therapeutic regimen and lifestyle changes are factors which have been described with particular focus on the aetiology, complications, natural history and risks pertaining to the disorder. Expansive data depict that type 2 diabetes incidence and prevalence increase rapidly to the detriment of pecuniary measures in health services and society. Recent decades have been encumbered with tumultuous and contentious polemics marked with conflicts in research findings and budget cuts in the awareness, prevention, treatment and control of the constraints and challenges regarding diabetes and related conditions, especially in LIMCs. Our health systems are faced with adverse policy expansiveness to unavoidable or threatened accelerating global needs in health and development as well as a realizable paradigm of performing more with less. Strategies in the prevention, treatment and control of type 2 diabetes and diabetes-related conditions aim to mitigate the risk of the development of diabetes and its complications.

Index terms— cardiovascular diseases; dipeptidyl peptidase-4 inhibitors; insulin analogues; lignans, phytoestrogens, lifestyle changes.

1 Introduction

ype 2 diabetes constitutes a chronic metabolic aberration with global increasing prevalence and untoward sequelae in vulnerable populations. It is rapidly reaching epidemic proportions in certain countries, especially the non-industrialised nations; and exacerbating the already extant healthcare burdens of poor countries. With no defined cure for diabetes, therapeutic modalities have involved dietary regimen, lifestyle modifications, overweight and obesity management, as well as pathophysiologically type 2 diabetes-related therapeutic approaches (Olokoba et al., 2012). Even with the provision of diverse treatments in industrialized countries, numerous type 2 diabetes subjects do not achieve glucose control (Higgins et al., 2016). Modalities for the prevention, treatment and control of type 2 diabetes and diabetes-related conditions aim to mitigate the risk of the development of diabetes and its complications or the attendant sequelae in susceptible and vulnerable populations due to the urgency in the exacerbation of the disorders and global acceleration in diabetes incidence and prevalence. Diabetes is a priority issue of urgent concern; if not adequately stemmed, culminates in elevating the burdens on health systems and society.

Recent decades have been encumbered with tumultuous and contentious polemics marked with conflicts in research findings and budget cuts in the awareness, prevention, treatment and control of the constraints and challenges regarding diabetes and related conditions, especially in LIMCs This paper tends to address the convergence in therapeutic and other measures for the prevention, treatment and control of diabetes and its complications which will aid in the reduction of the prevalence, morbidity and mortality as the resultant impact of diabetes mellitus. Type 2 diabetes prevalence has been found to exacerbate as a result of inadequate awareness, prevention, treatment, control and advocacy for a healthy lifestyle (Tiwari, 2015;Liu et al., 2016).

2 II.

3 Dietary Carbohydrates

Evidence from prospective observational research and clinical trials converge to undergird the significance of selected dietary patterns, foods and nutrients to prevent and manage type 2 diabetes. The quality of dietary carbohydrates and fats consumed is more vital than the abundance of these macromolecules as micronutrients. Inasmuch as enormous progress has been enacted in the development and implementation of evidence-based nutrition guidelines or recommendations in industrialized nations, it is pertinent to promote and enhance concerted worldwide efforts and policies to mitigate regional differences (Ley et al., 2014).

The health impacts of the use of dietary carbohydrates are of concern to everyone as regards the glycaemic index (GI), glycaemic load (GL) and glycaemic response (GR). Cognizance has been given to postprandial glycaemia in the health spectrum, with GI as a reliable and predictive instrument in the classification of carbohydrate diets in this instance. Consumed foods with reduced GI and GL are necessary to prevent, control and manage diabetes and coronary disease, and may be extrapolated to obesity, while transient to moderately marked associations were detected in certain oncological disorders (Augustin et al., 2015). A consensus was reached that diets low in GI and GL ought to be contextually considered as healthy in characterization of carbohydrate foods, with fibre and whole grain content which are important for insulin resistance patients (Augustin et al, 2015). The current global epidemic of obesity and type 2 diabetes has increased simultaneously with adverse metabolic events. There is expansive evidence that the type of carbohydrate consumed is important in the development or prevention of insulin resistance, obesity and the metabolic syndrome. Due to the prevalence of overweight, obesity and insulin resistance, increased concerns for the quality and carbohydrate type consumed promulgate the perception that carbohydrate diets are liable to exacerbate rather than mitigate cardiometabolic risk, with divergent views regarding their glycaemic index and fibre levels as pertinent in the management of chronic diseases.

4 III. Lipid-Associated Parameters

There is widespread evidence that the type of carbohydrate consumed is vital in the development and prevention of obesity, insulin resistance, the metabolic syndrome and diabetes-related events; with other measures to control carbohydrate-lipid interactions as they impact on diabetes and obesity (Chukwuma Sr, 2017a). Investigations of the impact of serum markers of cholesterol synthesis and absorption in type 2 diabetes incidence revealed an associated risk with the presence of type 2 diabetes, invariably ascribed to insulin sensitivity (de Mello et al., 2015). Cholesterol synthesis was related to greater incidence of type 2 diabetes, while cholesterol absorption correlated with lower incidence of type 2 diabetes, with detection of a genelifestyle interaction on markers of cholesterol absorption. There is a linkage of increased risk to develop insulin resistance and type 2 diabetes. In obese subjects, it is realized that adipose tissue releases elevated concentrations of non-essential fatty acids, proinflammatory cytokines, glycerol, hormones and risk factors which are connected in insulin resistance development. With concomitant presentation of dysfunctional pancreatic islet beta cells in insulin resistance, the resultant impact is deranged control of blood glucose abundances (Khan et al., 2007).

In this wise, a vast majority of subjects were diagnosed with hypoalphalipoprotenaemia (HA) during routine lipid profile determination (Schwab & Uusitupa, 2015;Vibhuti, 2016). This can be employed as an independent factor in the assessment of coronary artery disease risk and further management. The fundamental objective for HA management and associated lipid aberration is the reduction or atherosclerosis risk that culminates in increased morbidity and mortality. There are numerous aetiologies for low HDL cholesterol contents, and certain of these, such as type 2 diabetes, elevated triglycerides, obesity, overweight, and deficient physical exercise are related to insulin resistance. Also, implicated in low HDL content are high carbohydrate consumption, cigarette smoking, progestational drugs, anabolic steroids and beta blockers.

In an identical trajectory, ApoA-1 has the potential to undergo oxidative alterations which decrease anti-atherogenic function of HDL; elevated methionine sulfoxide (MetO) concentrations in ApoA-1 in premature MI and type 2 diabetes patients; with concomitant increased MetO concentrations in ApoA-1 leading to HDL dysfunction (Sartore et al., 2015). Thus, ApoA1 undergoes oxidative alterations which mitigate anti-atherogenic functionality of HDL in selected young subjects with CHD, and type 2 diabetic with no significant correlation in all parameters in healthy subjects. Elevated ApoA-1 levels are predictive of CHD or CAD. Type 2 diabetes results in dyslipidaemia, such as augmented triglyceride concentrations and decreased HDL contents which are established risk factors for coronary artery disease. Results show that increased concentration of ApoA-1 are not reflective of the glycaemic status, and are independent of increase in LDL: HDL ratio suggestive of disparate metabolic pathways and the genetic association for LDL and ApoA-1 (Singla et al., 2009).

IV.

5 Lignans, Phytoestrogens, Carotenoids

Lignans are polyphenols food micronutrients obtainable in plants. The lignan precursors are contained in an expansive variety of plant-based foods, such as fruits, legumes, seeds, vegetables and whole grains. The flaxseeds constitute the richest dietary resource of lignin precursors. On consumption, lignin precursors undergo conversion to the enterolignans, enterodiol and enterolactone by bacteria which conventionally inhabit the intestine of humans

(Lampe, 2003;Rowland et al., 2003). Lignan-rich diet constitute portion of a healthy dietary regimen, that the functionality of lignans in the prevention or mitigation of hormone-associated oncological disorders is not pellucid. Lignans constitute the major source of dietary phytoestrogen in traditional Western diets (de Kleijn et al., 2002;Valsta et al., 2003). Studies suggest that phytoestrogens have anti-diabetic activity via both estrogen-dependent and oestrogen-independent pathways, with consideration that food sources, such as soy and whole flaxseed constitute portions of total

6 , 2007).

There is ample evidence that carotenoids mitigate diabetes risk because of their anti-oxidant attributes. A study (Sluijs et al., 2015) demonstrated that elevated contents of beta-carotene and alpha-carotene in diets have relationships with decreased incidence of type 2 diabetes in the healthy population. Diets with elevated concentrations of beta-cryptoxanthin, lycopene, lutein and zeaxanthin have no relationship with type 2 diabetes risk; and the relationships between dietary carotenoids and type 2 diabetes risk are not altered due to the smoking status of the subjects.

V.

7 Alcohol Consumption

An assessment of the association between alcoholic intake and type 2 diabetes incidence suggested that moderate consumption of alcohol was related to a decreased risk of type 2 diabetes development (Marques-Vidal & Vollenweider, 2015). In the study, no protective influence was associated between alcohol ingestion, and impaired fasting glucose because there was no defined association of type 2 diabetes and the quantity of intake. The study suggested that moderate alcohol intake is not associated with reduced risk of developing superimposed type 2 diabetes and impaired fasting glucose. Other findings demonstrate that associations between alcohol drinking frequency is associated with diabetes risk; and that alcohol consumption within three to four weekdays is connected with the lowest diabetes risk, even when incorporating average weekly alcohol intake; but taking into consideration ethnic background, family history, overweight and age (Burns, 2017).

8 VI.

9 Cardiovascular Concerns

The lowering of glucose by anti-glycaemic drugs in the early stages of type 2 diabetes may be beneficial in patients with cardiovascular disease and cardiac failure; although, it is class-dependent rather than on the resultant impact of glucose lowering. Certain classes of antiglycaemic drugs are prone to cause or elicit cardiac failure; but this is not undergirded by enough evidence (Kappel et al., 2015). Evidence stipulates that merely early intensive risk factor control can modulate CVD morbidity and mortality in subjects presenting with type 2 diabetes. A study (Catalan et al., 2015) detected a high preclinical atherosclerosis prevalence of carotid plaque presence and burden in new-onset type 2 diabetes patients, with predilection for women. Prompt intervention is effectual to prevent CVD and possibly reverse pre-clinical atherosclerosis. Carotid intima media thickness was exacerbated in new-onset diabetes in comparison to matched controls, with significant prevalence more elevated in new-onset diabetes. HbA1c and atherogenic dyslipidaemia partly explicate these disparities. Glycaemic control optimization by employing a basal plus insulin approach by inducing a significant decrease in HBA1c profoundly improved HRV parameters correlating with sympathetic and parasympathetic functionalities; thus suggesting stringent glycaemic control employing insulin for the improvement of cardiovascular autonomic activities in type 2 diabetes (Maadjhou et al., 2017).

In addition, adiponectin is a vital adipocytesecreted adipokine with insulin-sensitizing and antidiabetes attributes (Kadowaki et al., 2006). In contradistinction to several pro-inflammatory adipokines/cytokines secreted by adipose tissue, the plasma levels of adiponectin are reduced in obese persons and patients presenting with type 2 diabetes, hypertension and cardiovascular disease. Other than these metabolic functionalities, adiponectin impacts several protective influences against cardiovascular disorders, such as diabetic cardiomyopathy (Shibata et al., 2004), myocardial infarction (Shibata et al., 2005) and stroke amelioration (Nishimura, 2008). The protective influence of adiponectin diabetes vascular complications is partly due to its property to counteract hyperglycaema-mediated reduction in available circulating endothelial progenitor cells which are causally connected with diabetes cardiovascular complication (Chang et al., 2010).

Extant data reveal strong positive correlation of high resting cardiac rate and risk of type 2 diabetes (Aune et al., 2015). Although, resting heart rate is predictive of cardiovascular disease risk, its association with diabetes remains inconclusive, especially in non-Western ambient (Zhang et al., 2010). An elevated resting cardiac rate was detected to be independently related to high risk of type 2 diabetes in women; and the association of high cardiac rate with increased BMI, BP or WHR measurements are connected with a significantly augmented risk. However, cardiac rate has been limited potential as a marker for the screening of patients with undiagnosed type 2 diabetes in rural areas (Li et al., 2014). Also, elevated allostatic load score, ALS is a determinant of the biologic response to stress, but its relationship with the risk for diabetes and cardiovascular disorders in the African migrant population has not been deciphered (Utumatwishima et al., 2017a). ALS measurement portends a valid

costeffective trajectory for the detection of diabetes and cardiovascular disease risk in the African population. Dipeptidyl Peptidase-4 Inhibitors, Insulin Analogues, Antidiabetic Therapeutic Agents

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Speculations are rife regarding the role of Dipeptidyl peptidase-4 (DPP-4) inhibitors in type 2 diabetes treatment, but DPP-4 inhibitors decrease HbA1c, albeit, to a magnitude less than sulfonylureas, with no production of weight gain or hypoglycaemic risk (Monami et al., 2010). Type 2 diabetes exhibits progressive dissipation of beta cell functionality, thereby necessitating usage of orally active DPP-4 inhibitors, such as sitagliptin and vildagliptin. DPP-4 inhibitors present certain theoretical advantages greater than extant therapies having oral antidiabetic compounds, but amenable to or compliant with selected patients (Richter et al., 2008). MACE rate is not elevated in the presence of DPP-4 inhibitors, thus undergirding the CV safety and compliance of these newfangled antidiabetic therapeutic agents. The application of TECOS suggests that high cardiac failure hospitalization resulting from saxagliptin is not related to class effect of DPP-4 inhibitors. It may be that an evening injection with NPH insulin in combination with an extant maximal therapy with metformin and sulfonylurea can be simple, effective and well-tolerated first-choice strategy by, or patients desiring oral medication (MDedge, 2004). Short-acting insulin secretagogues may be employed in fasting diabetic patients with predominantly postprandial hyperglycaemia **??**Bashir et al., 2015). Oral DPP-4 inhibitors constitute an alternative to sulfonylureas for diabetes patients during fasting due to their glucosedependent mechanism of action, efficacy and tolerance, as they cause moderate HbA1c decrease, and being non-weight dependent, and have very low hypoglycaemic risk.

Incretinomimetics constitute novel type 2 diabetes drugs which increase glucose-induced insulin production. This drug class comprises two subclasses: Exogenous Glucagon-like Peptide analogues, GLP1a, such as liraglutide and the Dipeptidyl peptidase-4 inhibitors which elongate the half-life of endogenous GLP1, such as vildagliptin. These two subclasses do not exhibit significant disparities on insulin sensitivity and insulin secretion following two weeks of treatment in type 2 diabetes subjects (Well et al., 2017). Incretin-based regimen for therapeutic provisions in type 2 diabetes patients modify diverse aspects of the disorder, such as hypersecretion of glucagon, aberrant gastric evacuation, postprandial hyperglycaemic, and rarely, pancreatic beta-cell dysfunction. DPP-4 inhibitors, gliptins augment glucagon-like peptide-1 (GLP-1) provision and modulate "incretin defect" observed in type 2 diabetes patients (Godinho et al., 2015). Good glycaemic control with minimal hypoglycaemic risk or any aberrant effects have been reported, irrespective of pancreatitis reports which have not been clearly defined. Research is aimed at the extant capability of DPP-4 inhibitors in enacting putative pancreas functionality, especially regarding the inhibition of apoptotic pathways and inducement of beta-cell proliferation. Also, other cytoprotamine impacts on certain organs/tissues which are more associated with adverse type 2 diabetes complications, such as cardiac, renal and ophthalmic perturbations have been demonstrated (Godinho et al., 2015;Dungan et al., 2017). They do not cause hypoglycaemia unless combined with therapeutic regimen that can cause such effects. The mechanism of DPP-4 inhibitors is to elevate incretin (GLP-1 and GIP) concentrations (McIntosh et al., 2005) causing the inhibition of glucagon release, leading to increased insulin secretion, with decreased gastric evacuation, and decreased blood glucose concentrations, accompanied by marginal statistically significant exacerbation of heart failure (Wu et al., 2014). There is extant warning that alogliptin, linagliptin, saxagliptin and sitagliptin as type 2 diabetes medications are liable to cause adverse, severe and disabling joint pain (USFDA, 2016). However, there are other minimal comparative utility evidence versus other therapeutic agents concerning other DPP-4 inhibitors, such as omargliptin and trelagliptin administered onceweekly (Stoimeni et al., 2017). The utilization data of glucagon-like peptide 1 (GLP1) receptor agonists and DPP-4 inhibitors in clinical practice showed that incretin prescriptions have been conducted in numerous cases extraneous to the regulatory limits; but appropriate utilization of incretins provided commensurate results and benefits as in pivotal trials (Montilla et al., 2014).

11 VIII.

12 Combination Therapy

The choice or selection and application of a glucose lowering drug depend on the severity of hyperglycaemia, hepatic and renal-related functionalities, hypoglycaemic risks, body mass index, blood glucose self-monitoring ability and cost-benefit analysis of available therapeutic regimen. Type 2 diabetes treatment modality involve a variety of prevailing therapeutics, such as sulfonylureas and nepaglimide which augment insulin secretion, troglitazone that induces increased insulin action in fat and muscle, metformin augments insulin action in fat and muscle; while miglitol and acarbose enact retarded carbohydrate absorption from food consumption, respectively (Buse, 1999). The drugs enacted for type 2 diabetes treatment pose significant side effects or adverse risks, whereas other combinational therapy of insulin and sulfonylureas decrease the daily insulin requirement (Riddle, 1996), insulin and metformin combination therapy (Golay et al., 1995), and troglitazone-insulin in combination effectually lowered insulin requirement and promoted glycaemic control (Buse et al., 1998). The application of combination therapy is congruous for subjects presenting with type 2 diabetes because they frequently exhibit poor responses to single-drug therapeutic regimen. Metformin and troglitazone have similar and beneficial impacts on glycaemic control in type 2 diabetes patients. Metformin functions basically by reducing endogenous glucose formation, while troglitazone accelerates peripheral glucose disposal rate. Basal insulin analogues present

decreased hypoglycaemic risk in comparison to NPH insulin, but hypoglycaemia persistently constitutes a major stumbling block for the achievement of recommended fasting plasma glucose targets in diabetic subjects (Russell-Jones et al., 2015; Chukwuma Sr, 2017b). Insulin degludec consistently achieved lower FPG concentrations when compared to insulin glargine. Reduced nocturnal rates established that hypoglycaemia manifested with insulin degludec, probably due to prolonged action and insulin degludec flat profile. Thus, the lower rate of nocturnal established hypoglycaemia observed with insulin degludec compared to insulin glargine culminates in a decreased mean FPG fasting plasma glucose, especially in type 2 diabetes patients. It was detected that HbA1c and fasting glucose are inadequate as screening diabetes measurement in an African migrant population (Utumatwishima et al., 2017b). With the increasing diabetes epidemic in Africa, one of the main challenges is the accurate assessment of the presenting asymptomatic persons affected. In recent decades, the OGTT is recognized as a diagnostic norm for diabetes detection, but it is expensive and time-consuming, thus necessitating an option for a single blood test, such as HbA1c and fasting plasma glucose. The elevated prevalence of both haemoglobin C trait and sickle cell trait, SCT may obscure HbA1c diagnostic value. Also, in populations of African descent, FPG functionality may be objectionable as a marker of asymptomatic diabetes. On that score, the magnitude of African diabetes may be submerged due to constraints and challenges in the provision and identification of feasible hyperglycaemic markers.

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14 IX.

15 Discussion and Conclusion

Diabetes is a significant endocrine and metabolic phenomenon and disorder associated with mortality and morbidity with astronomical health system and socioeconomic pecuniary embarrassment. It is pertinent to continuously implement, monitor and evaluate population-based interventions and registries which prevent diabetes, provide modalities for its early detection, utilization of lifestyle and therapeutic interventions in the prevention and/or retardation of its attendant sequelae or progression to untoward complications. A study (Chukwuma Sr, 2017c) has attempted to develop and improve the welfare and well-being of vulnerable populations in the interactions, comorbidities or co-occurrence for other diseases with diabetes. It is imperative to compare trends in diverse countries and regions, and coordinate progress towards the global target to stem the exacerbation of diabetes prevalence by 2015 as at 2010 (WHO, 2015; NCD, 2016).

The factors which are indicted for possible population level alterations in type 2 diabetes prevalence include combinational forces in personal attributes, and environmental risk factors or geneenvironment interactions (Chukwuma Sr, 2014), the detection effect, the evolutionary process of diabetes and global changes (Thibault, 2016). Also, it is important to engage in a healthy lifestyle among adults with type 1 diabetes for quality control of cardiometabolic risk factors, such as body mass index, body composition (IDXA), blood pressure, glycated haemoglobin, lipids, waist circumference, with insulin resistance as estimated glucose disposal rate (Schwab & Uusitupa, 2015).

The awareness, prevention, treatment and control of diabetes need to be integrated with those of other non-communicable diseases. We need to reduce obesity by augmenting physical activity, intake of vegetables, legumes, fruits, cereals, whole grains, particularly of high fibre presence, and decreased intake of fats. Effective and efficient intervention strategies focused on the specific needs of the population are required to stem the increase of diabetes prevalence and incidence. Information systems for baseline data evaluation, monitoring, evaluation and implementation are needed for screening and metabolic control of patients to improve diabetes care. This paper, therefore, proffers the consensus for actions to prevent, treat and control diabetes, diabetes-associated conditions with attendant sequelae, and including determination of lifestyle changes. These strategies are clear and congruously accepted as constraints and challenges in the convergence of the prevention, treatment and control of type 2 diabetes in the clinical setting and in the real world.

In the current environment, the values to ensure equitable and justifiable utilization of scarce resources in preventing, abating and controlling the epidemic of diabetes and related disorders have become increasingly important. Researchers and several wellmeaning institutions have been delivering rigorous unbiased evidence to advance rights, enhance quality and improve lives which will aid governments and agencies for the improvement of programmes and policies for the assurance of the global convergence on the constraints and challenges in the awareness, prevention, treatment and control of type 2 diabetes and related conditions. [1] [2]

[1]Convergence on the Constraints and Challenges in the Awareness, Prevention, Treatment and Control of Type 2 Diabetes and Diabetes-Related Conditions © 2017 Global Journals Inc. (US)

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