Review Article

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Pathophysiological Carbohydrate-Lipid Interactions in Covid-19, Obesity, and Diabetic Individuals

Chrysanthus Chukwuma Sr*

Executive Director, The Chrysanthus Centre for Future-Oriented Studies, Nigeria

ABSTRACT

The extant COVID-19 pandemic has resulted in an expansive mortality due to the SARS-CoV-2. The SARS-COV-2 is encompassed by a lipid bilayer that enhances fusion of the viral membrane to the host cell, replication, endocytosis, exocytosis and role of lipid metabolism in viral infectivity. In the absence of appropriate drugs and vaccines, there are never-ending opportunities for antiviral treatments. Consumption of diets suffused with carbohydrates and saturated fats contribute to obesity and diabetes prevalence, oxidative stress and comorbidities development as risk factors for COVID-19 pandemic as an emergency public health enigma. COVID-19 outbreak has invariably constituted a severe challenge to global public health system with resultant deficient approaches to stem the disorder but carbohydrates may provide accelerated diagnostics, appropriate, effective and efficient vaccines and therapeutic regimen. This paper provides a set of themes and modalities for analysing carbohydrate-lipid interactions as extrapolated to the issues and challenges of SARS-CoV-2, the causative agent of the COVID-19 pandemic.

KEYWORDS: Metabolism; Treatment; Diet; SARS-COV-2; Mortality; Vaccines

INTRODUCTION

The present global epidemic of obesity and type 2 diabetes has increased concurrently with debilitating metabolic episodes. There is expansive carbohydrate consumed is vital in the status of insulin resistance, obesity, and the metabolic syndrome.

There is scarcity of published data on the combined effects of interactions between micronutrients, carbohydrates and lipids. However, there are numerous data undergirding the be carbohydrates and lipids in diverse processes of energy balance and diseases.

Adequate measure is pertinent to control carbohydrates on obesity and diabetes. Investigation of the impact of foods and nutrients as complimentary strategies on COVID-19 treatment, recovery [1], restoration and sustainability [2] are evident despite the intricate complexity of the disease, scarcity of veritable vaccines [3], emerging variants of concern [4], syndemics or comorbidities [5] geopolitics and gain-of-function research [6,7].

Associated Factors in Exacerbating Obesity and Diabetes

The current COVID-19 pandemic with its associated variants depict clinical findings with several risk factors for adverse morbidity, sequelae and mortality in susceptible and vulnerable persons presenting diverse risk factors, for instance, obesity and diabetes with resultant untoward trajectory of COVID-19 [8]. The presenting epidemic of obesity and type 2 diabetes globally have exposed metabolic perturbations crucial in etiological mechanisms. Diet is a potent functionality in modulating metabolic syndrome expression that is associated with the levels and varieties of carbohydrates and fats as well as their interactions as significant parameters [9]. Insulin a resistance is relevant in the metabolic syndrome as a result of relative insulin failure to influence the numerous biological impacts on the Metab. There is deficiency of published data on the combined impacts on interaction between the micronutrients, dietary fats and carbohydrate valid data supporting the beneficial effects of both fat and carbohydrates moieties on various processes of energy balance metabolism

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Address for correspondence: Chrysanthus Chukwuma Sr, Executive Director, The Chrysanthus Centre for Future-Oriented Studies, Nigeria

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mechanisms manifest how the quality of dietary carbohydrate can affect weight gain by the absorption rate or the magnitude of carbohydrate. Evidence shows that the carbohydrate type is vital to the variability of insulin resistance, obesity, and the met taken into consideration to prevent, control and treat the presenting condition [10,11]. Diabetes constitute a metabolic disorder characterized by chronic hyperglycemia and immune-mediated type 1 diabetes, insulin-resistant type 2 diabetes, gestational, genetic, environmental, infectious, behavioral or drug-induced impairments [12], and in syndemics or comorbidity relationship with obesity [13,14]. Evolutionarily, the adaptation of living organisms has been as nutrient sources, such as carbohydrates, lipids and proteins. However, carbohydrates and lipids constitute the two major micromole storage compounds for energy generation. Significantly, the anabolism and catabolism of these macromolecules are inextricably linked in organs concerned with nutrient regulation, such as the brain, liver, adipose tissue, pancreas and muscle [15]. The rate of obesity has accelerated globally, thus I social burden per quality of life.

Pathogenesis and Pathophysiological Issues

It has not been easy to present a defined trajectory for carbohydrate and lipid metabolism as well as the extant but elusive interactions. It has animals conserve lipids from carbohydrates, but obversely detected in plants and, not practically present in animals [8]. In conventional carbohydrate-lipid interactions are not clearly pellucid, but the extant perturbations in diabetic metabolism depict these interactions are not clearly evident, but the perturbations extant in diabetic metabolism manifest these interactions. Carbohydrate or lipid is utilizable as the major source of body fuel; However, the metabolic trajectory varies in chemical processes and functionalities. It is manifest in the low as in severe diabetes and starvation that lipids are essential for body fuel, and it is also exhibited in the blood and internal organs, particularly the hepatic organ [12,16]. On detecting that there is diminished carbohydrate required for metabolism, depot lipid is accepted by the ketone bodies, and peripherally in burned in the muscles exclusive of carbohydrate metabolism [15]. This occurs as a normal process, Diabetic obesity is commonly observed at the initial stage and soon after insulin therapy. Apparently, hyperglycaemia enhance determined in unique features of lipemia, diabetes and lipodystrophy. Lipaemia is obvious in two opposite metabolism phases:

a. anabolic is directed for storage and

b. catabolic in the storage flow to the hepatic organ for disease manifestation [16]

The evidence is inter alia fatty enlargement of the hepatic organ in diabetic children that may quickly disappear during control and treatment, even in chronic ketosis condition. As evidenced in high-income societies, an increase prevalence predisposes to pathophysiological events which culminate in non-alcoholic fatty liver disorder that worsens acute hepatic organ derangement to concomitant cirrhosis and oncological hepatocellular degeneration [17]. Changes in insulin response, beta-oxidation, lipid transport and storage disruption established disequilibrium in chemokines and nuclear receptor signaling are indicted in these variations. Insulin, adipokines stimulate pathways which regulate the activities of key enzymes of metabolism control in the integration of organismal carbohydrate and lipid metabolism. Defined overnutrition dysregulates these extant pathways with perturbative sequelae leading to insulin resistance and type 2 diabetes [17]. The diabetes and insulin resistance correlates with aberrant lipid and carbohydrate metabolism. Obesity development is a complex process connected with genetic susceptibility and environmental factors that is not clearly elucidated [18]. Lipid aggregation in inflammation and ER stress is clinically evident in liver regeneration and hepatic oncological derangement [19]. The subclass of diabetes characterized as not insulin-responsive or dependent, NIDDM depicts insulin resistance and hyper-insulinaemia, with resultant glucose intolerance, hyperglycaemia and fulminant diabetes and comorbidity of ketosis and obesity [13]. In these perspectives, it is pellucid that obesity and dysfunctional metabolic disposition are defined risk factors for noncommunicable diseases, such as type 2 diabetes which may be compounded with coronavirus disease 2019 or COVID-19 [20].

Genetic and Environmental Factors

Persons in advanced age, comorbidities and vulnerable populations are susceptible to COVID-19 as these factors are inextricably-linked to genetic, epigenetic, environmental and interaction variables [21] in obesity and diabetes. Obesity is a crucial aspect of metabolic syndrome, leading to type 2 diabetes development metabolic syndrome with nonspecific aetiology for the increase in incidence. This may be influenced genetically in the prevalence of these disorders [22,23]. It has not been clearly determined how genetic variables have interactions with environmental and dietary aspects to accelerate their incidence [22,23]. metabolism, including glycan biosynthesis, pathways in the metabolism of cofactors and vitamins, ubiquitin mediated proteolysis, pathways of signal transduction, interactions of neuroactive ligand-receptor, pathways of nervous system, and neurodegenerative perturbation pathways are upregulated in obesity in comparison to normal persons [24]. Obversely, genes associated with molecules of cell adhesion, cytokine-cytokine receptor interaction, insulin signaling and immune system pathways are downregulated in obesity. Genes processing and manifestation of antigen, complement and coagulation cascades, axon guidance and pathways of neurodegenerative disorders history of diabetes in distinction to diabetic subjects without any family history but not in diabetes devoid of any family history [24]. Obversely, gene proteolysis, signal transduction, insulin and PPAR signaling pathways are downregulated in persons with diabetes and concomitant family history.

It is evident that genes connected in inflammatory pathways are disparately expressed in both obesity and type 2 diabetes. These findings are indicative that genes associated with carbohydrate, lipid, and amino acid metabolic pathways, neuronal function and inflammation are significant in obesity and type 2 diabetes pathology. Genetic predisposition contributes immensely to obesity as determined by familial aggregation, twin and adoption studies [22,23]. Obesity results from energy intake, mainly accumulated as triglycerides surpassing energy expenditure [24]; and influenced by age, diet, developmental stage, genes and physical activity [25]. The prevalence increase of obesity correlates with type 2 diabetes prevalence, impaired glucose tolerance [26] and numerous complications of both disorders, such as arthritis, hypertension, sleep apnoea, cardiovascular disorders and organ perturbations [27]. As a result of the increase in obesity and diabetes prevalence, it is perspicuous that future life expectancy of affected subjects is likely to decline [28].

Oxidation and Metabolism

The pathogenic SARS-COV-2 has the potential to enhance metabolic alterations during viral infection that promotes its survival, changes in cell morphology with concomitant inflammation and tissue damage, and alterations in glucose and lipid metabolism [29]. Competition for respiration among substrates in animal tissues is depicted is evident in the Glucose Fatty Acid Cycle of the reciprocal metabolic linkage between glucose and fatty acids. The generation of glucose storage, with the inhibition of fatty acid oxidation. The availability of free fatty acids predisposes to fatty acid oxidation and oxidation, with inhibition of glucose oxidation and augmentation of glucose storage during depletion of glycogen reserves [30]. Evidence exists that fatty acid oxidation inhibits glucose production in liver with defined enzyme mechanisms. A permissive latitude for fatty acids during insulin secretory response of islet beta-cells is notable as a protective mechanism in continuous availability of respiratory substrate. Extended duration in islet beta-cell exposure to fatty acids diminishing the insulin secretory response to glucose and prevailing mechanisms. Fatty acid oxidation is connected with impairment of deficit information in fatty acid functions in the depletion of glucose storage or glycogen deposition. Type 2 diabetes depicts glucose storage inhibition resulting in protracted augmentation of plasma FFA I humans and experimental animals is connected with glycogen depletion; in contrast, glucose storage inhibition in type 2 diabetes is related to glycogen reduction [30]. The defined functionality of fatty acids in impaired carbohydrate metabolism in type 2 diabetes paves way for future research.

Combustion pervades life, and intensive studies culminate in fuel substrates which are essential for sustenance, are in competition and interaction among themselves for respiratory combustion. Numerous features of imminent mutual interaction that is exhibited in both reciprocal and dependent characteristics between glucose and lipid metabolism have been elucidated [31]. These include

a. The inhibitory effects of elevated levels of fatty acids on glucose oxidation through inactivation of mitochondrial pyruvate dehydrogenase.

b. The inhibitory effects of enhanced glucose content on fatty acid oxidation via malonyl-CoA regulation of fatty acid ingress into the mitochondria and

c. The stimulatory impacts of exacerbated glucose abundance on de novo lipogenesis, lipid synthesis from glucose by SREBP1c glycolytic and lipogenic enzyme regulation and lipid metabolism to thermogenesis functions as a modulating mechanism that governs intramyocellular lipid homeostasis culminating in contributing to skeletal muscle protection against lipotoxicity [32-34].

The rate of lipid oxidation may correlate with concentration of plasma free fatty acids contents. Lipid contribution to energy expenditure is greater in obese as compared to control subjects. This is usurped by lipids in the energy metabolism of both diabetic and no n-diabetic obese individuals, and it is the resultant impact of their elevated fat contents. The concomitant decline in carbohydrate metabolism ostensibly results as sequelae to variations in glucose tolerance, with resultant retarded glucose storage and oxidation in the obese subject [35]. In normal pregnancy, it has been realized that plasma triglycerides are elevated 2-3 fold. Deficiency of a significant impact of diabetes, body weight, and augmented carbohydrate intake on blood lipids during gestation differentiates pregnancy from atherosclerosis-associated hypertriglyceridemia's and relates to a distinct physiologic regulatory mechanism [36].

Carbohydrate and lipid metabolism is markedly dependent on mitochondria regulated by NRF-1 [37]. The metabolic pathways are controlled via metabolic variations at levels of high energy substances, such as AMP/ATP and the NAD+/NADH ratios. Reduced levels of ATP activate AMPK that elicits the activation of eclectic transcription factors, NRF-1, that regulates both carbohydrate and lipid metabolism. Conversely, alterations in the NAD+/NADH ratios influence the activity of other metabolic regulators like the sirtuins which are protein deacetylases [37]. Sirtuins augment the activity of transcriptional co-activator, PGC-1 via deacetylation, the major co-activator of NRF-1. Further research is required to determine if sirtuins directly regulate NRF-1 activity in relation to carbohydrate and lipid metabolism.

COVID-19 infection as exemplified in varied infections induces an inflammatory response that is usually restricted to the respiratory system, but in fulminant episodes, an expansive proportion of the body is overwhelmed [38]. Thus, obesity has been associated with chronic oxidative stress, and dietary restriction and weight dissipation have resulted in remarkable decrease in oxidative stress indices within a short span of time [39].

Diet, Control and Therapeutics

As exemplified above [38,39], dietary approaches and strategies are pertinent in diabetes and obesity management. Stringent dietary regulation with minimal carbohydrate diet has been extensively applied, that later subsided with novel applications of medications. The major objective has been to ameliorate dietary fat intake in order to obviate the atheriosclerotic disease risk, with less attention on carbohydrate quality and abundance. With exacerbating obesity and diabetes globally, the trend and target are on the diet micronutrient composition. Low carbohydrate diets have been effective in initial weight mitigation and glycaemic control improvement, with long-run acceptance and deteriorating lipid profile [40]. Modulations of extremely reduced carbohydrate contents involve restricting saturated fat and augmenting both carbohydrate and lipid. Decreasing saturated fat is ostensibly the key to reduce low-density lipoprotein, LD2 cholesterol with retardation of adverse impacts of conventional very low carbohydrate diets. Augmented dietary protein predisposes satiety, decreased energy intake and concomitant improved glycaemic homeostasis, but devoid of substandard improvement in glycaemic regulation or cardiovascular sequelae regarding the impact of weight loss. Type 1 diabetes has responded to regulatory effects with low carbohydrate diets, without ketosis and hypoglycaemic complications. Carbohydrate-restricted diets exhibit effective weight reduction as low fat diets; and fat substitution for carbohydrate is invariably advantageous concerning cardiovascular disease risk without need for weight loss; and improves metabolic syndrome characteristics [41]. Low carbohydrate diets are dependent upon mechanisms of glucose directly or indirectly via insulin that is a major regulatory component in gluconeogenesis, glycogen metabolism, lipogenesis and lipolysis.

Studies have assessed the relative impact of fat compared to carbohydrate and the distinctiveness among fatty acids and variants of carbohydrates on insulin resistance and related risk factors for diabetes, cardiovascular disease and obesity. The fibre content of

the carbohydrate diet ostensibly provides advantages regarding diabetic control, while lower cholesterol and postprandial blood glucose are connected with viscous fibres [42]. Resting energy expenditure and measurement of both carbohydrate and lipid oxidation rates as well as measurements observed in both fasting and parenterally fed states were determined [15]. Although, there were no variations in resting energy expenditure, a significant decrease $p<0.05$ in RQ 5% and carbohydrate oxidation rate, 24% accompanied by a concomitant exacerbation of lipid oxidation rate, 42% was detected in parenteral nutrition in fusion. There were no disparities in plasma insulin, glucose, and insulin resistance observed in pre- and post-infliximab [17]. Improvements in insulin resistance following anti-TNF-alpha therapy have been observed in inflammatory states in children, but no alterations were detected in adult patients presenting with Chron's disease [43].

There is growing evidence that dietary plant polyphenols are potential nutraceuticals and supplementary treatments for type 2 diabetes due to their biological attributes, such as high concentration of phytochemicals and antioxidant capacity [44] Findings from in vitro, animal models and human experiments indicated that plant-food polyphenols, and polyphenol-rich products

a. Attenuate dyslipidaemia, hyperglycaemia and insulin resistance,

b. Potentiate adipose tissue metabolism,

c. Mitigate oxidative stress and stress-sensitive signaling pathways and inflammatory responses [45], as well as

d. Modulate carbohydrate and lipid metabolism. Polyphenols can contribute to the prevention and abatement of long-term diabetic sequelae, such as cardiovascular disorder, nephropathy, retinopathy and other predisposing factors [46,47]. At the molecular level, carbohydrates are intricately linked with immune components. Thus, carbohydrate-based systems potentially constitute features to combat COVID-19 [48]. In addition, carbohydrates depict antifungal, antimicrobial and antiviral attributes which make them propitiously relevant to morphologically engage SARS-COV-2 in the provision of vaccines and therapeutic agents.

DISCUSSION

Diabetes constitute a metabolic disorder characterized by chronic hyperglycaemia and immune-mediated type 1 diabetes, insulin-resistant type 2 diabetes, gestational, genetic, environmental, infectious, behavioural or drug-induced impairments [12] It is generally postulated that obesity and type 2 diabetes have escalated in prevalence globally with concomitant sequelae or complications in morbidity and mortality. The pathophysiology [49,50] or pathobiology of these conditions have been difficult to unravel or elucidate. Several hormone-like signaling agents which influence energy metabolism are emitted from adipocytes, such as leptin, as well as immature cells, such as tumour necrosis factor-alpha. Obesity and type 2 diabetes present marked gene-environment interaction [51]. Paucity of data is extant on the single-gene defects which result in these states, but in several instances, polygenic contributions have been detected [10,52]. The impact of the extant COVID-19 pandemic on present and future human growth and development perspicuously depends on inter alia the socioeconomic correlates with pertinence to ideologically behavioural imprint, macromolecular interactions, birth weight, obesity, diabetes, cardiovascular disorders and other communicable and noncommunicable diseases as also evident in SARS-COV-2 or COVID-19 perturbations [53-57].

CONCLUSION

Numerous environmental states including foetal ambience, lifestyle and social diversions have been implicated in the predisposition of these ailments or disorders. Fundamentally, an imbalance between caloric ingress and energy dissipation elicits endocrine and/or metabolic responses exacerbating the age-dependent dysregulation in lipid and carbohydrate metabolism in vulnerable populations and COVID-19 susceptible individuals.

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