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Review Article



A review of ketogenic diets and their potential impact on COVID-19: Is there an interaction?

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Abstract

The aim of this review is to explore the potential significance of ketogenic diets (KDs) in the treatment and prevention of coronavirus, specifically focusing on their beneficial impacts on inflammation, immune responses, and the respiratory system. The study reviewed several COVID-19 observations and findings, particularly those concerning obesity as a contributing factor. As per the study, notable obesity is linked to an elevated chance of intensive care unit (ICU) admission requiring invasive mechanical ventilation in individuals with COVID-19. Additionally, the increasing weight gain associated with a SARS-CoV-2 infection prognosis may be attributed to various factors, including prolonged systemic inflammation, susceptibility to acute respiratory infections, and the influence of the viral disease. The article ultimately concludes that ketogenic diets may play a pivotal role in managing and preventing SARS-CoV-2 by diminishing the virus's impact on inflammatory responses, immune functionality, and respiratory system health. Furthermore, the article focuses on the link between extreme obesity and severe COVID-19 results, implying the need for weight control in high-risk patients.

Keywords: Ketogenic Diets, COVID-19, Intensive Care Units.

Introduction

The COVID-19 virus, caused by those infected with it, has caused a pandemic since March 2020, spreading globally and causing new outbreaks of the disease. In general, the casualty rate stood at 2.3% (Wu et al., 2020), while Italy has recorded a total of 2,343,069 COVID-19 cases with 80,253 fatalities (3.4%) (Assoc, 2021). The rate of mortality of the COVID is intently attached to the seriousness of aggravation virulence factors as well as the presence of underlying health conditions such as obesity, diabetes, hypertension, and ongoing obstructive pneumonic illness. These elements increment the gamble of creating diseases (Yang et al., 2020). Glycogen plays a role as a stored carbohydrate in both the liver and muscles. It acts as the source of fuel for high-intensity activities (>80% VO₂max). Provides readily available energy. To maintain muscle during activity and competition while ensuring an optimal glycogen level, it is recommended to follow a high carbohydrate diet (6 g/kg/d1). The liver can only

hold 100 grams (to 400 calories) of glycogen whereas skeletal muscles have a larger capacity ranging from 300 to 700 grams (800 to 2800 calories). To avoid fatigue and diminished performance caused by glycogen depletion it is advisable to consume carbohydrates. Hence it is practice to make modifications that aim to preserve glycogen levels during workouts (Thomas et al., 2016).

The COVID-19 epidemiology tool

Early investigations of COVID-19 suggested that the source of the virus may have been the Huanan Seafood Wholesale Market (HSWM). A study of 425 initial cases revealed that during the outbreak's earliest stages, the estimated reproduction number (R₀) was 2.2 (Li et al., 2020). Another modelling study found the R₀ value to be 2.68. A third study, considering the prevention measures put in place by the Chinese government, proposed the effective R₀ was 3.1 at the start of the epidemic, but may have decreased with time

(Wang et al., 2020). The virus responsible for causing COVID-19 is known as SARS CoV 2, which is classified as the strain of coronavirus known to affect humans (Franchi et al., 2012). A few different types of COVID that have a high death rate are SARS CoV and MERS CoV (Zhu et al., 2019). Scientists categorize coronaviruses into four groups according to their makeup: α CoV, β CoV, γ CoV, and δ CoV (Su et al., 2016). Further studies revealed that the new virus is part of the β -CoV family (Forni et al., 2017). The infection takes 1–14 days to incubate, but it commonly takes 3–7 days (Su et al., 2016). Fever, weariness, dry cough, headache, nasal congestion, joint discomfort, muscular soreness and sore throat are common symptoms in mild to moderate cases (Forni et al., 2011; National Health Commission, 2020 and Yang et al., 2020). In a study involving 1099 individuals diagnosed with coronavirus, it was discovered that 43.8% experienced fever symptoms at the onset of their illness. This percentage increased to 88.7% while they were receiving care after being discharged (Chen et al., 2019). It should be noted that older individuals or those with weakened systems may not exhibit fever symptoms (Wang et al., 2020). An examination of the first 425 verified COVID-19 cases suggested that the outbreak had a R0 of 2.2 at the start (Li et al., 2020). At the commencement of the pandemic, a phase-adjusted assessment of the epidemic dynamics showed an effective R0 of 3.1 (Wu et al., 2020). It appears that early cases had a different detection pattern that was linked to a common source at Huanan Seafood Wholesale Market, with these cases eventually developing via person-to-person transmission (Wang et al., 2020).

Virological features of SARS-CoV-2

The incubation period for COVID-19 is 1–14 days, and most patients who are mildly to moderately ill experience symptoms such as fever, exhaustion, and a dry cough. Headache, runny nose, sore throat and myalgia are common in children with the illness (O'Brien et al., 1993). Many patients report nausea, diarrhoea and vomiting as well. Another study conducted during a COVID-19 outbreak observed that 43.8% of patients had fevers when their illness started, and this percentage rose to 88.7% while they were in the hospital (Reilly et al., 2017). Notably, elderly individuals or those with compromised systems exhibited radiological and neurotic characteristics in the early stages of infection: an intricate lung pattern accompanied by protein-rich exudates, clear alveolar edema, responsive lung cell hyperplasia, and mild inflammatory infiltration. Gross examination revealed that every lung showed superficial and widespread congestive symptoms, with somewhat hemorrhagic rot, as well as cut surfaces. On rare occasions, people with missed may not have fever (Guan et al., 2020). Leukopenia is a frequent laboratory anomaly in COVID-19 patients, occurring in 83.2% of cases and being more prevalent in severely sick patients. Prior research has also found increased dimer levels and a prolonged prothrombin time in individuals with severe illness (Tian et al., 2020; Xu et al., 2020).

Lifestyle choices can have a role in COVID-19 risk factors

Even though the current death rate is 2.3% (Wu et al., 2020), the sudden surge in the number of people affected by COVID-19 created significant challenges for the healthcare systems of many countries, resulting in a high number of fatalities. Different investigations have shown an association between Coronavirus fatalities and more established age (O'Brien et al., 1993), as well as the presence of previous circumstances like diabetes, coronary illness, and hypertension. Obesity has additionally been related with kidney illness (CKD) (Wu et al., 2020). Since these circumstances are affected by way of life decisions, focusing on them is significant. Taking action against these risk factors mentioned earlier is vital for increasing satisfaction and reducing health impacts from future products (Wang et al., 2020).

The COVID-19 stage's two antagonists are hyperglycemia and obesity

During the SARS-CoV-2 infection, obesity is a known prognostic of the necessity of intensive care and a significant risk of death (Narici et al., 2020). In accordance with this, this represents a significant shift in the COVID-19 disease's severity. Obesity in children and adolescents has been well established. Obesity affects a number of important functions, including an increased vulnerability to COVID-19 (Kalligeros et al., 2020). Obesity impairs breathing by altering diaphragm excursion and affecting immunity. responses to viral infection (Muscogiuri et al., 2020), which has an impact on whether a person develops a chronic illness. Low-grade inflammation worsens oxidative stress and glucose intolerance, all of which have detrimental effects on cardiovascular health (Paich et al., 2013).

Diabetes and the danger of the Coronavirus

Hyperglycemia is autonomously connected with an expanded hazard of mortality from cardiometabolic diseases, especially when it is within the range of non-diabetics (Honce and Schultz-Cherry, 2019; Kumar et al., 2009; Kwong et al., 2011). Concentrates also back up the importance of hyperglycemia for coronavirus-related consequences. For example, among 605 Coronavirus patients with fasting blood sugar levels (FBG) between clinic confirmation and taking 28-day in-clinic problems, the adjusted OR was 2.61 (95% CI 1.64-4.41) for the range of 6.1-6.9 mmol/l. in contrast to those with an FBG level of 6.1 mmol/l (Narici et al., 2020). Moreover, even after adjusting for prior diabetes mellitus, fasting blood glucose (FBG) on confirmation was independently associated with fatal 30-day outcomes (severe respiratory distress syndrome, multiple organ failure, ICU admission, septic shock, or death) among 461 Coronavirus patients treated at six clinics in Guangdong, China.

The investigation analyzed how KD impacts the blood sugar curve and determined a value of 0.817% (with a 95% confidence interval spanning from 0.765 to 0.868). We

determined that the critical blood glucose threshold is 6.23 mmol/L, indicating a level. KD has the ability to alter how the system works by causing a shift in M1 macrophages metabolic preference from glycolysis to phosphorylation when they are activated. This transition leads to an increased production of cytokines and chemokines such, as IL 1b, TNF a and IL 6. It has been seen that the presence of glucose diminishes the development of M1 macrophages while advancing the development of M2 macrophages in people determined to have Coronavirus. In addition, it has been seen that hydroxybutyrate (OHB) actually prevents the actuation of NLRP3 inflammasome by hindering the arrival of K⁺ from macrophages, in this manner, the depicted phenomenon in Fig. 1 involves the deliberate avoidance of inflammasome assembly (Luigi et al., 2022).

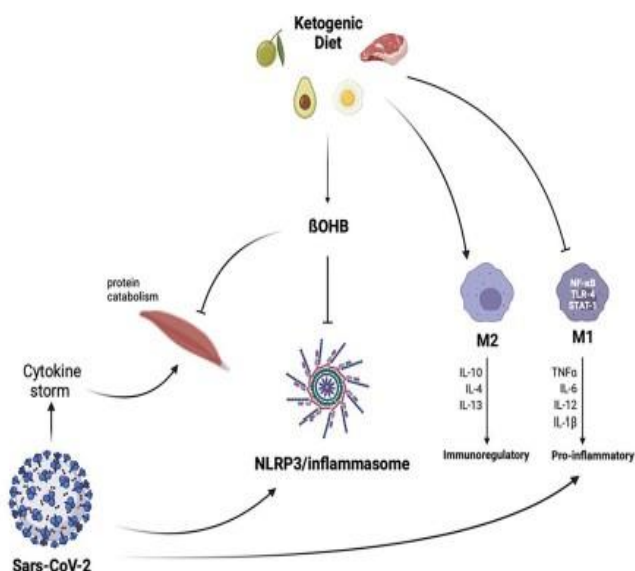


Fig. 1 Ketogenic diets have variable effects in the treatment of SARS-CoV infection. A ketogenic diet strongly inhibits the development of M1 and simultaneously triggers the development of M2. In addition, oleic acid also inhibits activation of the NLRP3 inflammasome and has anti-catabolic effects on human skeletal muscle. Beta-hydroxybutyrate is shorthand for a ketogenic diet (Luigi et al., 2022).

The COVID 19 pandemic has resulted in a number of individuals affected by the virus. However, it is crucial to distinguish between the health consequences arising from SARS CoV 2 infection and the impact of the pandemic on those who have contracted the virus. Following the SARS outbreak, in 2003 medical professionals observed a proportion of individuals who continued to experience symptoms after recovering from illness for an extended period. For example, as indicated by a study, nurses in Toronto, Canada, encountered challenges in resuming their employment. In

order to develop a comprehensive comprehension of COVID-19, it is imperative to analyze the enduring consequences it has on both individuals who have contracted the virus and those who have not been infected (Honce and Schultz-Cherry, 2019; Kumar et al., 2009; Kwong et al., 2011).

Ketogenic diet

Ketogenic diets have been utilized since the 1920s for treating epilepsy. Have extended their application to incorporate metabolic issues, headaches, malignant tumors, and outrageous weight. Carbohydrate ketogenic diets (VLCKDs) are a compelling weight reduction technique for individuals with serious fatness and cardiovascular infection who need to lose weight rapidly. They entail limiting carbohydrate intake while increasing fat and protein intake, with a daily calorie intake of 800 kcal (Wilder, 1921; Paoli et al., 2013).

VLCKDs require adequate nutritional conditions and lean mass, but weight loss is predominantly due to fat mass loss. VLCKDs are effective in controlling blood glucose, as the extremely low carbohydrate intake leads to significant decreases in blood sugar and improved glycemic management (Caprio et al., 2019; Gomez-Arbelaez et al., 2018). Obese individuals exposed to VLCKDs for a brief period have demonstrated improved function, with type 2 diabetes benefiting more than could be attributed to weight loss alone. An abrupt reduction in carbohydrate consumption decreased glucose production in the liver, resulting in increased insulin sensitivity in the liver (Luukkonen et al., 2020; Reilly and Saltiel, 2017).

Using a ketogenic diet as a lifestyle behavior to combat COVID-19

Dietary guidance has received little attention in public health talks on avoiding or mitigating the risk of SARS-CoV-2 and its sequelae. Combining medium-chain triglyceride supplementation and intermittent fasting has been indicated as a beneficial treatment to promote good dietary choices, an immunological response, and anticipated clinical results (Lim et al., 2011). The ketogenic diet can modulate both intrinsic and adaptable immune cells, which collaborate to protect the host from pathogen attacks. The recognition pattern of receptor activation of the viral antigens modulates innate immune cells, triggering proactive defenses and preventing viral multiplication (Soliman et al., 2020). The NLRP3/inflammasome is a critical sensor of innate immunity that controls inflammation of virus, and acetoacetate and beta-hydroxybutyrate have been shown to inhibit its activation. A ketogenic diet can decrease blood glucose spikes, oxidative stress, and circulating inflammatory indicators in animals and humans. It can actuate the hydroxycarboxylic receptor 2, which diminishes atomic component kB by raising the degrees of hydroxybutyrate. The utilization of sugars like carbs, starches, and basic sugars assumes an urgent part in deciding blood glucose levels (Bowie and Unterholzner, 2008). Notwithstanding, the dietary rules in numerous countries

advance an eating regimen that is low in fat yet high in sugar. Tragically, this kind of diet can aggravate hyperglycemia (Lim et al., 2011; Soliman et al., 2020).

Invulnerable Framework, Coronavirus and Diet Ketogenic

The transmembrane serine protease 2 (TMPRSS2) and a spike protein of SARS-CoV-2 can access lung cells, avoiding blocking by angiotensin-converting enzyme 2. This results in the infection of pulmonary epithelial cells, which can cause pyroptosis and the release of damage-associated molecular patterns (DAMPs). Macrophages and monocytes are then activated of cytokines that are released. When the immune response is weakened, it is possible for abnormal infiltration of monocytes, macrophages, and lymphocytes to occur. This situation can be further aggravated by an increase in blood vessel permeability and the occurrence of storms. These storms involve substances like IFN-gamma, IL-6, IL-2, IL-10, and granulocyte colony-stimulating factor (G-CSF). Symptoms such as inflammation, pneumonia, emphysema, and widespread pneumonia can be observed (Huang et al., 2020).

KDs, lockdowns, and the coronavirus

Both the high-fat, ketogenic diet (HFKD) and very low-calorie ketogenic diet (VLCKD) are considered significant treatments and should be administered under strict clinical management due to the presence of side effects. However, it may be difficult to monitor individuals undergoing a ketogenic diet during the pandemic's forced isolation. Ketogenic diets may lower the likelihood of the cytokines, the most pathogenic feature of COVID-19 marked by elevated levels of C-reactive protein (CRP), interleukin (IL)-6, oxidative damage, redox state, and cell death. This study focuses on the chronic low-grade inflammatory phenotype (CLIP), which underlying several metabolic syndrome-related illnesses. It has been connected to depression and is required for the prediction of respiratory indicators (Yang et al., 2020; Huang et al., 2020; Tay et al., 2020).

Viral Infections, Immunity and Ketogenic diet

Recent research suggests that there is evidence indicating a link, between an increase in body weight and the susceptibility to contracting infections, including the H1N1 virus and the seasonal flu (Kossoff et al., 2020). During the outbreak of the H1N1 flu researchers made an observation regarding how obesity could impact hospitalization and mortality rates. A study (Kwong et al., 2011) revealed a correlation between obesity and higher rates of hospitalization and mortality among individuals affected by the virus. This discovery shed light on how obesity might influence the severity of H1N1 infections emphasizing the need for investigation in this field. It is worth noting that health conditions associated with weight, such as blood pressure, abnormal lipid levels, and prediabetes could potentially play a role in this matter. These conditions can increase the likelihood of events and infections. Moreover, they have the potential to contribute to heart

dysfunction and kidney failure thereby increasing the likelihood of organ failures associated with pneumonia (Simonnet et al., 2020). Furthermore, obesity has been associated with inflammation, which can result in issues (Li et al., 2020). Research has shown that obese diabetic rats and overweight individuals have experienced inflammation in their lungs (Mancuso, 2010; Elliot et al., 2019). The accumulation of fat in lung tissue and airways can cause inflammation and hinder wound healing during an infection. Studies on animals have demonstrated the way that flu contamination can cause expanded protein loss, oxidative pressure, and pneumonic edema (Pascarella et al., 2020).

Respiratory Function and the Effect of Low-Carb Ketogenic Diets

There is evidence suggesting that diets with high content and low carbohydrate intake can affect certain parameters. However, important consuming unnecessary carbs can likewise have results. Exceptionally low-sugar ketogenic consumes less calories are not exhorting for people who are obese. In 40 healthy people, two distinct ketogenic diets, HFKD and VLCKD, were found to reduce CO₂ generation without reducing oxygen intake (Foster et al., 2010). In addition, a comparison of the VLCKD to a diet such as a Mediterranean diet showed VLCKD significantly reduced the ratio of respiratory exchange and increased energy expenditure (Foster et al., 2010; Rubini et al., 2015).

KDs in COVID-19 Supportive Care

In COVID-19 models, studies in mice revealed that HFD-induced ketone bodies have a positive effect (Wang et al., 2020; Luukkonen et al., 2020). In intensive care units (ICUs), high-fat ketogenic diets (HFKDs) have been explored as a potential treatment option for mechanically ventilated patients. The initial results have been promising (Mohamed et al., 2019; Sukkar and Bassetti, 2020). Moreover, telemedicine has presented encouraging results in the treatment of individuals with epilepsy using HFKDs. It has demonstrated promising safety and compliance measures, suggesting that it could be an option when faced with quarantine or strict isolation. Several writers have advocated KDs in COVID-19 management based on these factors, and certain clinical trials are currently underway (Paoli et al., 2020). In severely obese patients, VLCKD organization may be viewed as a viable adjuvant treatment for COVID-19 and, more importantly, as a preventive for rapid weight loss (Paoli et al., 1989).

The Potential of Ketogenic Diets for COVID-19 Management

Recent scientific findings have suggested that a ketogenic diet (KD) may be a promising strategy for the treatment of COVID-19. It is well-established that the SARS-CoV-2 virus targets the respiratory system primarily, with individuals with underlying health conditions, notably obesity and diabetes, identified as a high-risk group for enduring severe COVID-19

outcomes (Kalligeros et al., 2020; Kass et al., 2020). Obesity has been associated with an increased likelihood of necessitating hospitalization and experiencing COVID-19-related complications (Simonnet et al., 2020). Concerning these factors, KDs, which are known for their capacity to prompt digestion and changes in digestion, have arisen as a potential way to deal with treatment. The enlistment of ketosis by means of a KD might have various helpful impacts, for example, the tweak of safe reactions (Paoli et al., 2020), a decline in irritation (Sukkar and Bassetti, 2020), and an upgrade of glucose digestion (Rubini et al., 2015). These effects are of particular significance in the scenario of COVID-19 management, where an excessively aggressive inflammatory response, also known as a cytokine storm, has been linked to disease severity (Tay et al., 2020). Moreover, it is noteworthy that a KD may impart benefits by enhancing lung functionality and optimizing respiratory effectiveness (Sue et al., 1989; Paoli et al., 2020), qualities that could prove indispensable in COVID-19 cases. Recent clinical observations and research efforts have provided evidence that KDs may indeed contribute to the amelioration of hyperglycemia, reduction in the severity of cytokine storms, and improvement of metabolic health in COVID-19 patients (Sukkar and Bassetti, 2020; Paoli et al., 2020). Consequently, there exists a compelling rationale for the pursuit of further investigative efforts and clinical trials aimed at substantiating the efficacy of KDs as an adjunctive therapeutic modality in the comprehensive management of COVID-19 (Luigi et al., 2022).

Conclusion

This review of ketogenic diets and COVID-19 suggests interesting research and clinical trials. Ketogenic diets may help treat and prevent COVID-19, but more research is needed to prove this. Extreme obesity and unfavorable COVID-19 results highlight the need of weight management and appropriate lifestyle choices, particularly in high-risk individuals. Understanding and treating comorbidities like obesity and diabetes is crucial to designing successful pandemic prevention and treatment methods. Ketogenic diets may reduce the cytokine storm and improve respiratory function in COVID-19 patients. However, ketogenic diets should not be recommended to those with respiratory failure or certain medical disorders without medical supervision. Dietary therapies, including ketogenic diets, should be addressed in a complete COVID-19 management plan that includes immunization, public health recommendations, and early identification and treatment. Medical professionals, researchers, and governments must work together to adopt evidence-based COVID-19 interventions and mitigate its long-term effects. Interdisciplinary investigations on nutrition, immunology, and viral infections will help determine the COVID-19 advantages of ketogenic diets. Ketogenic diets for severe COVID-19 patients should be tested in well-designed clinical studies. Scientific investigation and evidence-based medicine can help us make educated public health choices as we face and overcome this unprecedented epidemic. We can

build a robust future against viral epidemics and other global health challenges by combining medical knowledge, creative research, and a focus on human health and well-being.

Conflict of Interest

The author hereby declares no conflict of interest.

Consent for publication

The author declares that the work has consent for publication.

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