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Commentary

Unlocking the potential: Keto diet's impact on immunity, obesity, neurodegenerative diseases, and cardiovascular diseases

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Commentary

An ancient proverb like "we are what we eat", entails the significance and an influence of dietary habits and thereby nutrients on all living beings. A universal system encompasses various categories of classes that recognize consequences of various diets on immunity and thereby on the health of an individual [1,2]. These mechanisms mainly consist of epigenetic machineries, metabolic pathways, circadian rhythms, and diet-responsive effectors [3-5]. In this light, various clinical studies exhibit immune-modulatory and beneficial effects of interceding nutrients on various diseases [6-9] (**Figure 1**).

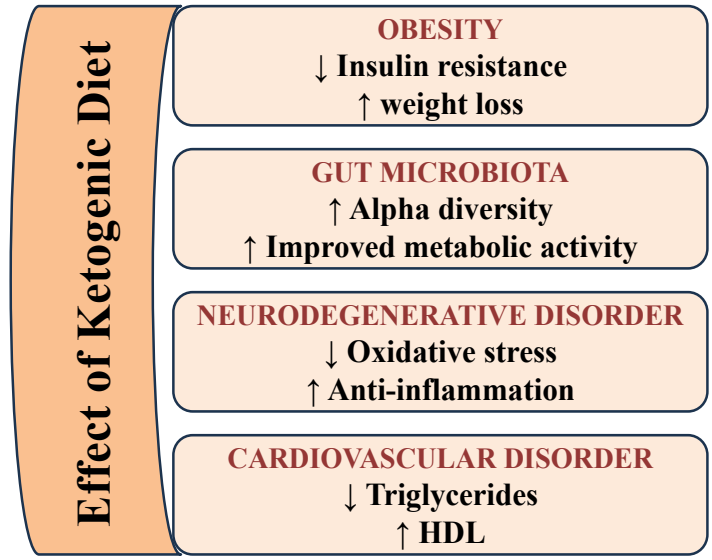

Figure 1. Effect of ketogenic diet on various disorders.

Obesity

Excessive nutrients intake hastens advancement in numerous disorders, particularly in obesity and type 2 diabetes. A rate of occurrence of plethora of metabolic syndromes, like cardiovascular disease (CVD), and cancer, are directly proportional to the obesity [10]. To fight against the comorbidities, related to obesity, dietetic intermediation is a favorable technique [11]. In recent years, ketogenic diets have been acquiring an upsurge of relevance for their anti-inflammatory properties [12]. In 2022, Barrea et al., examined a 31-day active stage Very low-calorie ketogenic diets (VLCKD) effect on a data set of 260 women that ranged in age group between 18 to 70, with BMI of 25.0–50.9 kg/m^2. This study reported the decrease in BMI, as well as in high sensitivity-CRP levels recorded on the Day 31 [13]. Lorenzo et al. studied an immune profile of 79 obese patients along with 32 fit volunteers as the control group for a weight reduction therapy centered on VLCKD, balanced hypocaloric diet (LCD) or bariatric surgery (BS). The results reinforced the immunomodulatory outcome of ketosis stimulated by keto diet to recover innate-immunity and to preclude diseases and carcinogenesis in obese patients [14].

Gut Microbiome

One of the most recent data implies a substantial role of KD in modification of the gut microbiome to recover the disease condition, based on discrete increase in the percentage of *Bacteroidetes* to *Firmicutes* (B/F) and decrease in *Proteobacteria* [15]. In 2022, Daniel et al. reported advantageous effects of yogurt intake in an obesity-linked type 2 diabetes dietary mouse model with respect to safeguarding the glucose homeostasis, deterrence of liver steatosis as well as imparting hepatic insulin resistance [16].

Neurodegenerative Diseases

Multiple sclerosis (MS) is one of the most common inflammatory diseases of the CNS that has a potential to transform into advanced disabilities and infirmity. The genetic as well as environmental elements can lead to MS. More number of MS cases are found in western countries [17]. One of the reasons is the western diet that contains high levels of carbohydrates and fats which augments insulin secretion and higher inflammation. Forsythe et al., reported the efficiency of 12-week (KD) in reducing the insulin resistance and decrease in numerous inflammatory markers in patients [18]. KD has exhibited anti-inflammatory and neuroprotective properties to cure patients with various pediatric and neurological ailments. In diseased conditions, brain cells face vigorous challenges to withstand homeostasis. In such cases, KD has demonstrated the metabolous crosstalk within CNS and brain's periphery to control neurological diseases. KD causes upregulation of astrocytic adenosine kinase (ADK) enzyme to enhance levels of anti-inflammatory molecule, adenosine, which also reduces the levels of TNF-α, IL-6, and CXCL2/3. In a disorder like West syndrome (WS), Patients experience spasms and hypsarrhythmia, and eventually advance into a critical epileptic brain condition, Lennox-Gastaut syndrome (LGS). However, when hormonal therapy was merged with KD, treated patients were at low risk of developing the LGS [19].

Cardiovascular Diseases

There are 4 types of cardiovascular diseases, namely, Aortic atherosclerosis, cerebrovascular disease, peripheral artery disease, and coronary artery disease (CAD) [20,21]. KD's efficiency at improved cardiac function, cardiomyocyte survival, and decreased cardiac fibrosis has been recognized by many studies. It has exhibited significant efficiency in the regulation of lymphoid cells' differentiation and the T cell subsets. One research group assessed the mode of action of KD in treating diabetic cardiomyopathy [22]. This study found a decrease in the percentage of ST2L + cells in Tregs, IL-33 titers and lower ST2L ligand synthesis in the presence of ketone bodies. The activation of pro-inflammatory cytokines like IL-1 and IL-18 and caspase-1 is regulated by NLRP3 inflammasome upon sensing atherosclerosis. Thus, regulatory mechanism of the NLRP3 deactivation could assist in the treatment of several chronic disorders.

During the course of KD, many patients experience nausea, acidosis, and hypoglycemia. Although most side effects are manageable, the atypical ones that cause Parkinsonism, inflammation of pancreas, impairment in small intestines, and CVDs require immediate attention, cessation of the KD, and advance care to diminish negative consequences [23].

Matter of Concern

Although, ketogenic diet has shown instrumental role in the management of many health diorders, but the complexcity associated with it can be ignored. In general consumption of low carbohydrate alongwith high protein and fat diet may cause hike in LDL cholesterol and triglycerides which can cause detrimental health effects [24]. Apart from this, increased protein metabolism due to high protein consumption leads to increase in glomerular pressure and filteration [25]. Some researchers also suggested development of kidney stones due to high protein diet [26,27]. A reduction in bone mineral content is also reported after long-term consumption of ketogenic diet [28].

Conclusion

In summary, the ketogenic diet has attracted considerable attention due to its possible physiological advantages, such as promoting weight reduction and potential therapeutic uses. The present commentary provides a discussion on the effects of ketogenic diets on various illnesses. Based on the available literature, it is evident that the ketogenic diet exhibits potential for ameliorating obesity, cardiovascular illnesses, and neurodegenerative diseases. However, it is important to note that these beneficial benefits are typically transient in nature.

Future Prospectives

The ketogenic diet has garnered significant attention due to its potential effects on several health domains, encompassing immunity, obesity, neurological disorders, and cardiovascular conditions. Nevertheless, it is crucial to acknowledge that scientific research is a continuous and evolving endeavor, and subsequent discoveries may have been made subsequent to the aforementioned time period.

1. Future investigations have the potential to yield further elucidation about the influence of distinct facets of the ketogenic diet, such as its impact on the gut microbiota or metabolic pathways, on the immune system.
2. Researchers may investigate the potential synergistic effects of integrating the ketogenic diet with complementary therapy, such as behavioral therapies or pharmaceutical interventions, in order to optimize the efficacy of weight loss programs.

3. Further investigation could explore the underlying pathways by which ketosis and its effects on brain metabolism may contribute to the mitigation of neurodegeneration.
4. Although certain studies indicate potential improvements in risk factors such as triglycerides and HDL cholesterol, apprehensions have been expressed over the potential influence of this intervention on LDL cholesterol levels and long-term cardiovascular well-being. Subsequent investigations could be directed towards elucidating the aforementioned impacts and discerning the specific demographic that would derive the greatest advantages from adopting a ketogenic methodology.
5. As the knowledge around personalized nutrition expands, potential future developments for the ketogenic diet may involve customization according to individuals' genetic profiles, metabolic characteristics, and specific health objectives. The implementation of personalized techniques has the ability to optimize the effectiveness of the intervention while simultaneously mitigating the occurrence of potential adverse effects.

Author Contributions

VK provided the conceptualization. VAP, AT and VK wrote the original draft of the commentary. VAP, AT and VK performed writing-review and editing. All authors contributed to the article and approved the submitted version.

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Data Availability Statement

No new data were created or analyzed in this study.

Conflict of Interest

The authors declare no conflict of interest.

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