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REVIEW ARTICLE

EFFECT OF KETOGENIC DIET ON SELECTED CARDIOMETABOLIC-RELATED DISEASES

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ABSTRACT

Cardiometabolic diseases (CMD) describes a combination of metabolic abnormalities that increases the risk of type 2 diabetes, cardiovascular diseases, including pathological changes such as insulin resistance, hyperglycemia, non-alcoholic fatty liver disease (NAFLD), dyslipidemia, abdominal obesity, and hypertension. It is a multidimensional disease involving genetic, behavioral, and environmental factors, with increasing evidence that lifestyle changes and patient education can significantly reduce the risk of this disease. Cardiometabolic disease cannot be easily studied for morbidity due to its multifactorial nature. The study of comorbidity is an emerging field. NAFLD affects 32·4% of the world's population and 13.5% of Africans. Diabetes affects 463 million cases globally in 2019 were expected to increase by 51% in 2045; with a much higher increase of 143% expected in Africa. This affects 2.7 million adults in Nigeria, which is estimated to increase to 47 million by 2045. The total number of ischemic heart disease (IHD)-related deaths reached 9.14 million in 2019, accounting for 49.2% of all CVD-related mortalities. There are many strategies used to tackle each of the components of cardiometabolic syndrome. Conventional drugs have huge economic implications and side effects that most people in third world countries have not been able to circumvent. Fasting therapies have been proposed as a treatment for seizure disorders since the time of Hippocrates and were more formally adopted for the treatment of epilepsy in 1911 by the French physicians Guelpa and Marie. KD is a very low carbohydrate, high protein, very high fat content diet which induces ketogenesis. KD mimics prolonged fasting affect state resulting in upregulated ketogenesis. Ketone bodies are bioactive compounds that elicit molecular signals resulting in inhibition of histone deacetylase from expressing genes that upregulate lipogenesis and upregulation of acetylation involved in expression of genes that upregulate ketogenesis. It increases the particulate size of LDL, (HMG-CoA) reductase, increase lipolysis, HMG-CoA synthase 2, cataplerotic activity, upregulated sirtuins production, increase high-density lipoprotein, increased sirtuins production, hence eliciting therapeutic effect in the management of NAFLD, diabetes and cardiovascular disease.There is usually a mild side effects that are experienced with this therapy but can be overcome after four weeks or be treated with certain intervention. There is therefore

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a need to explore ways of incorporating KD in the clinical management and treatment of cardiometabolic diseases.

Keywords Cardiometabolic disease, Ketogenesis, Ketogenic diet, Ketone bodies

INTRODUCTION

There is a growing quest of what we should eat to maintain optimal health. This even becomes more imperative as communicable and non-communicable diseases soar, especially in developing countries like Nigeria. Nutritional emphasis has changed from the era of single nutrient to the current era which involves investigating the effect of dietary patterns like; Ketogenic diet (KD), vegetarian diet, Atkins diet, Mediterranean diet and western diet in relation to diseases. There have been myriad issues about the role of these dietary patterns and diseases[1].

Cardiometabolic related diseases are global health concerns that have resulted in huge loss of productivity and medical expenses. They include cardiovascular diseases, diabetes and hypertension. There has been compelling evidence to emphasize the nature of fat rather than just its composition. This raised the awareness that fat content does not translate to cardiovascular diseases. Rather, the composition determines the impact on cardiovascular health. The quest for novel ways of managing this is germane to ease the mortality rate and improve health outcomes. Many interventions have been employed including clinical trials on ketogenic diet which has resulted in improvement of cardiometabolic health. This review looks at the biochemical basis for such discoveries and possible ways to adopt a ketogenic diet[2].

Ketogenic Diet

Ketogenic diet (KD) is a very low carbohydrate, high protein, very high fat content diet which induces ketogenesis. In the year 1920, KD was developed and referred to as stimulated fasting. It was used to prolong fasting and hence reduce seizures. This practice was used for epilepsy from at least 500 BC.

The KD was invented in 1921 to imitate the alterations in metabolism caused by fasting, and it began to gain acceptance as a productive juvenile epilepsy treatment in the mid-1990s. Nevertheless, Dr. Wilder of the Mayo Clinic claimed that fasting could continue to be advantageous if ketonemia was produced in some other manner[3]. After effectively treating a patient with ketone bodies, Wilder coined the phrase ”ketogenic diet.” Later calculations demonstrated that children should consume 10-15 g of carbohydrates daily, 1 g of protein for every kilogram of body weight, and the remaining calories as fat daily. Woodyatt found that acetone can be produced when a subject is starved or consumes a diet that is excessively heavy in fat and low in carbohydrate[4].

The medium-chain triglyceride (MCT) diet, modified Atkins diet (MAD), low glycemic index treatment (LGIT) diet, and classic long-chain triglyceride (LCT) diet are the four types of KDs that are now available. The shorter fatty acids are quickly digested compared to LCTs, which causes more ketones to be produced per calorie. Less total fat is required in the MCT diet as a result of the increased ketogenic potential, allowing for increased protein and carbohydrate intake as well as a larger variety of foods[5].

The MAD has no constraints on protein, water, or calories and has a 1:1 to 1.5:1 ketogenic ratio, which makes the diet more pleasant and meal planning simpler. This diet's main goal is to assist kids with behavioral problems who are reluctant to follow the conventional KD. The LGIT calls for substituting low-GI foods for high-GI ones, such as most refined carbohydrate, meat, dairy, certain unprocessed whole-grain products, and some fresh fruits and vegetables. Although the mechanisms of action of LGIT include both constant glucose levels and a reduction in glucose metabolism, ketosis is not always the result. As a result, these various diet options, such as the MAD and LGIT, may be appropriate for adolescents and adults and initiated as outpatients or used with limited resources, such as dietitians in resource-limited lesions[3].

Types of Ketogenic Diet

Classic Long-Chain Triglyceride (LCT KD

The most traditional type of KD is the classic LCT KD. It contains a 4:1 fat-to-protein-to-carbohydrate ratio (in grams)[5]. It is the most frequently used in clinical settings[6].

Medium-chain triglyceride (MCT KD

The MCT (C6-C12) KD was developed in 1971. More ketone bodies are produced from MCT consumption than when LCT is consumed. Compared to the LCT KD, its diet ratios are more flexible. Additionally, there is clinical proof that the MCT and LCT KD are equally effective. However, gastrointestinal side effects are usually linked to the MCT KD[5,6].

Modified Atkins diet (MAD

It is based on the Atkins diet, a well-known weight-loss plan. It does not strictly adhere to the ketogenic ratio, ranging from 1:1 to 1.5:1 and occasionally reaching 4:1. Furthermore, there are no protein, hydration, or calorie restrictions with the MAD. Intake of carbohydrates is limited to 10-15 g/day for the first month, and afterwards it can be increased to 20 g/day[5,6].

Low glycemic index treatment

The treatment with a low glycemic index is based on the assumption that the KD's protective effect is dependent on stable glucose levels. It has a more liberal regimen with a low-carbohydrate composition to reduce glycemic spikes[5,6].

Ketogenesis

Acetoacetate (AcAc), 3-hydroxybutyrate (3HB), and acetone are the three ketones that are produced during the process of ketogenesis. The main metabolite, AcAc, is the source of the other two. Acetone is produced as a result of spontaneous decarboxylation of AcAc, which is easily exhaled, while its reduction produces the stable molecule 3HB.

Biochemistry of Ketogenesis

Under physiological conditions, acetyl CoA from fatty acid oxidation enters the tricarboxylic acid (TCA) cycle and then reacts with oxaloacetate to produce citrate. However, under KD-induced metabolic conditions, oxaloacetate is transported out of the mitochondria and used in the gluconeogenesis process. In this scenario, acetyl CoA synthesis greatly outnumbers oxaloacetate in the mitochondrial environment, and the former engages in a series of condensation reactions that are characteristic of ketogenesis. First, two acetyl CoA molecules combine to produce acetoacetyl CoA. A functionally irreversible and rate-limiting reaction catalyzed by HMG-CoA synthase 2 results in combination of acetyl coA with acetoacetyl CoA to form 3-hydroxy-3 methylglutaryl CoA. This compound dissociates to form KB, acetoacetate (AcAc), which is then reduced to BHB via a reaction facilitated by BHB dehydrogenase and involving the NAD^+/NADH couple as the hydrogen donor[7].

It should be noted that BHB levels in the circulation and tissues are much higher than AcAc levels, indicating that the former is the dominant KB. BHB and AcAc are exported into the circulation from the liver and ultimately imported by the brain, heart, skeletal muscle, and other tissues with high metabolic demands. Once in these body compartments, BHB is oxidized to AcAc by BHB dehydrogenase, which acts as a prime regulator of the mitochondrial NAD^+/ NADH ratio status. AcAc is then hydrolyzed to form acetoacetyl CoA and succinate in a reaction enabled by the enzyme succinyl CoA: 3-oxoacid CoA transferase, and the acetoacetyl CoA is then cleaved to yield acetyl CoA in a reaction catalyzed by thiolase. The acetyl CoA and succinate form substrates for the TCA cycle and complex II of the electron transfer chain (ETC), respectively[8]. This process may also result in the increased succinate dehydrogenase activity, as observed in rodents, after prolonged administration of the KD. The effects of the KD can be mimicked by taking KB supplements, and there is some evidence that the production of KBs in the liver, which occurs under physiological conditions, can be inhibited in such a scenario, though this is not universally accepted. KBs are metabolized at a considerably higher rate than glucose and enter the TCA cycle directly as previously discussed, thus bypassing glycolysis. Importantly, much evidence suggests that at levels normally induced by ketogenesis, glycolytic ATP generation diminishes and the generation of ATP by oxidative phosphorylation increases[9].

Influence of KD on the Epigenome

Epigenetics refers to changes in alterations in the genome that can modify and affect gene expression levels. Despite reports on the hereditary linkages, recent studies indicate that it can occur due to environmental factors. These changes are also reversible. The modifications can occur as DNA methylation, chromatin structure changes and histone modification. Histone modifications is the most prominent and occurs as; N-terminal of histone

tails acetylation, methylation, phosphorylation and ubiquitination[10] .

The majority of epigenetic modifications occur during early embryogenesis. Dietary factors further elicit epigenetic modifications later in life[11]. These effects may be beneficial or harmful. Black raspberries have dramatic effects on the microbiome (increased Lactobacillus, Bacteroidaceae, and anti-inflammatory bacterial species) as well as methylation patterns in the wingless/integrated (WNT) signaling pathway. They also boost butyrate production in the gut through fermentation. Therefore, it seems that diets high in particular nutrients can positively alter genes that improve cellular health in general. Regarding chronic and degenerative disease, the advantages of the ketogenic diet may be both curative and preventive[12].

Miller et al, argued that a state of nutritional ketosis will positively affect resistance to; oxidative stress, mitochondrial function and also upregulate bioenergetics proteins[13] . The ketogenic diet's mechanism of action might be due to increased levels of adenosine, which blocks DNA methylation and, thus, exerts an epigenetic change[8]. Epigenetics can be positively modified by; nuclear lamin architecture, telomere length reduction, DNA methylation, and chromatin structure. Butyl hydroxybutyrate (BHB) signaling inhibits endogenous class 1 HDAC inhibitors and is affected by environmental factors and cellular responses. It is not surprising that a ketogenic diet has been associated with higher levels of protective genes like Foxo3a expression and global histone acetylation[14]. Additionally, there is proof that BHB can affect aging and gene regulation in the hypothalamus directly through the new histone modification known as -hydroxybutyrolactone of H3K9.

In addition to being crucial for oxidative respiration, nicotinamide adenine dinucleotide (NAD) also functions as a cofactor for sirtuin enzymes and poly-ADP-ribose polymerase (PARP). Sirtuins and PARP play roles in gene expression, DNA damage repair, and fatty acid metabolism. The use of BHB as a source of energy results in a higher $NAD^{+/}$NADH ratio. This favours activity of sirtuins and PARP. The energy equivalent, NADH from BHB is lower compared to that from glucose. It therefore wastes energy [12]. As a result, the keto- genic diet produces too much NAD^{+}, which benefits the cell's redox status. The activity of sirtuins and other NAD^{+} dependent enzymes may benefit from this. In particular in the mitochondria, increased acetyl-CoA promotes both enzymatic and nonenzymatic protein acetylation, which enhances overall mitochondrial performance. The amount of free rad- icals and the efficiency of ATP generation in the mitochondria may both be improved by BHB produced by a ketogenic diet. The transcription factor NF-kB, which is known to con- trol the expression of multiple proinflammatory genes, is likewise inhibited by BHB. The pro-inflammatory response is thereby diminished. Similar to this, 1,3-butanediol, a pre- cursor to BHB, controls inflammasome expression by histone hydroxybutyrate, as a result, it reduces the expression of inflammation markers caspase-1, IL-1B, and IL-18[8].

MicroRNAs

MicroRNAs (miRNAs) are small non-coding RNAs that typically contain 20–22 nucleotides. RNA transcripts that are longer are transformed into miRNAs, which bindto

target mRNAs and regulate gene expression. A small number of miRNAs regulate about 30 to 80% of the human genome. Numerous miRNAs have been discovered in human adipose tissue and have recently been used as biomarkers for the disease since obesity is more prevalent in individuals. According to a recent study, lean persons and obese people had varying levels of expression of the number of circulating miRNAs. Hence, mRNA can be used to anticipate potential obesity-related problems and keep track of how well weight loss treatments are working. Additionally, miRNA-based therapeutic tools have been evaluated in preclinical investigations and clinical trials. MiRNAs have emerged as prospective therapeutic agents in recent years for a number of disorders[15].

The level of miRNA in the blood may be altered by specific dietary modifications. There may be relationships between miRNA, diet, and aging or age-related inflammation because many of them, like the Mediterranean diet, have been shown to prevent chronic degenerative diseases and have also been proposed as additional therapeutic options in a number of clinical conditions[16].

In animal models, caloric restriction (CR) has been shown to alter circulating microRNAs. Recent research looked at the levels of miRNA in the serum and tissues of mice given 40% CR for 28 days. CR mice had higher concentrations of miR-16-5p, miR-196b-5p, and miR-218-5p in their serum, spleen, thymus, colon, and stomach. The ability of MiR-16-5p to decrease the generation of inflammatory cytokines raises the possibility that CR may indirectly affect inflammation[17].

There have not been many human researches that have looked into how KD or VLCKD affect miRNA. In 2019, Profiling of miRNA in 36 obese people who received biphasic KD for six weeks showed that only three of the 799 circulating miRNAs (hsa-let-7b-5p, hsa-miR-143-3p, and hsamiR-504-5p) were altered in the study's analysis, and this association was sex-independent. These miRNAs have targets that were implicated in PPAR functional control, oxidative phosphorylation, cytokine signaling pathways, and insulin signaling. The same researchers have also demonstrated that miRNAs linked to anti-inflammatory and antioxidant signaling pathways are changed in obese people but revert to normal levels after KD[18].

Potential Benefits of KD

Ketogenic diet has a lot of benefits. These benefits include anti-cancer effects, microbiome, epigenome, diabetes, weight loss and cardiovascular disease.

Cardiometabolic Disease (CMD)

A group of metabolic disorders that increase the risk of non-alcoholic fatty liver disease (NAFLD), type 2 diabetes, obesity, and cardiovascular diseases (CVDs) are together referred to as cardiometabolic disease (CMD). Insulin resistance, hyperglycemia, dyslipidemia, abdominal adiposity, and hypertension are some of these pathological alterations[19].

There is growing evidence that lifestyle changes and patient education can dramatically lower the risk of this disease, which is a multifaceted condition combining genetic, behav-

ioral, and environmental variables[20]. It is simpler to quantify the morbidity of the individual cardiometabolic illness components than thecomorbidity.

Prevalence of CMD

Globally, 32·4% suffer from non-alcoholic fatty liver disease (NAFLD)[21] while Africans (13.5%) suffer from NAFLD[22]. Diabetes affected 463 million individuals globally in 2019 with a projected increase by 51% in 2045. There is a higher projection of 143% increase is expected in Africa. CVDs, a major cause of mortality globally, increased from 12.1 million deaths in 1990 to 18.6 million deaths in 2019[23].

Non-alcoholic Fatty Liver Disease

Non-alcoholic steatohepatitis and hepatocellular carcinoma risk are increased in NAFLD, a dangerous illness in which extra fat is deposited in hepatocytes, causing steatosis[22]. According to studies by Ezema et al. [23] and Riazi et al. [21], the prevalence of NAFLD in adults is expected to be 25.2% worldwide, ranging from 13.5% in Africa to 31.8% in the Middle East. North America has the lowest prevalence of 24.1%. Obesity and type 2 diabetes greatly increase the risk of NAFLD (43–92%) in these people [24]. De novo lipogenesis, which predominantly uses glucose as a precursor, lipolysis of stored triglycerides from adipose tissue, and dietary fats are the three sources of hepatic triacylglycerol. The majority of triglycerides (60–80%) in healthy individuals come from adipose tissue, 15% from food, and 5% from de novo lipogenesis. De novo lipogenesis-derived triglycerides are substantially more abundant (26%) in those with NAFLD. The production of fat from adipose tissue and de novo lipogenesis is accelerated by insulin resistance. Low-fat and low-carb hypocaloric diets were evaluated in a number of clinical trials with overweight or obese people, and equivalent decreases in intrahepatic fat were observed. Saturated fat, cholesterol, and animal protein intake which is high in ketogenic diets, which are all associated with insulin resistance, oxidative stress, and an increased flow of free fatty acids to hepatocytes[25].

Epidemiological studies suggest that NAFLD may be exacerbated by diets that are low in dietary fiber and omega-3 fatty acids, and high in; trans fat, simple carbohydrates, and animal protein (particularly from red and processed meat). In contrast to individuals who consumed the least animal protein, those who consumed the most were 54% more likely to have NAFLD (or 1.54, 95% CI, 1.20-1.98). A decreased risk of NAFLD is linked to whole grains, nuts and seeds, monounsaturated fats, omega-3 fatty acids, vegetable protein, prebiotic fiber, probiotics, resveratrol, coffee, taurine, and choline. According to the Tzu Chi Health Study, substituting fish or meat for one dish of soy raised the risk of developing NAFLD by 12–13%. Vegetarians had a 21% decreased risk of developing NAFLD, while whole grain consumption had an adverse connection with NAFLD. Dietary adjustments, weight loss, and physical activity are the mainstays of NAFLD treatment. Interventions in lifestyle that support weight loss have been proven to boost aminotransferase levels, enhance insulin sensitivity, and decrease liver fat. It has been suggested that entering a state of ketosis may help treat fatty liver, however there has been paucity of data to support this[25].

Effect of KD on NAFLD

Nonalcoholic fatty liver disease (NAFLD), a continuum of liver abnormalities including nonalcoholic fatty liver (NAFL) and nonalcoholic steatohepatitis (NASH), and can progress to liver cirrhosis and hepatocellular carcinoma.

Effect of KD on obesity

An increase in energy loss via heat and ketones in urine, sweat, and feces is caused by a decrease in metabolic efficiency. Due to enhanced lipid oxidation and mitochondrial respiration, it increases mitochondrial biogenesis and reduces the glycolytic process[6]. Ketone bodies have a diuretic and appetite-suppressing effect, which lowers calorie intake. KD's high fat content causes digestion to take longer, which makes an individual easy. More significantly, using fat as bodily fuel encourages fat loss, which in turn promotes weight loss[20].

There is ample proof that weight loss on the ketogenic diet is quite successful. It will cause weight loss, muscle maintenance, and decrease in other ilnness symptoms. Research also imply that the ketogenic diet is only better when the total calories consumed is equal. According to one study, participants on the ketogenic diet burn 2.2 times more fat compared to those on low-calorie, low-fat diets[26].

Diabetes

"A group of metabolic diseases characterized by hyperglycemia resulting from defects in insulin secretion, insulin action, or both" is how diabetes mellitus is described. In type 1 diabetes, an autoimmune response that destroys pancreatic beta cells causes inadequate levels of insulin and hyperglycemia. In type 2 diabetes, insulin resistance and decreased secretion of insulin by beta cells are the causes of these diseases. Retinopathy, nephropathy, peripheral neuropathy, peripheral arterial disease, and diabetic foot ulcers are among many problems associated with diabetes[27].

Type 1 Diabetes

Despite the fact that there is evidence that KD can lower blood sugar levels in children with type 1 diabetes, this population does not typically utilize them owing to the dangers of undernutrition, failure to thrive, decreased bone density, hyperlipidemia, poor sleep, amenorrhea, and hypoglycemia. Mood and conduct may also be impacted. Results in people with type 1 diabetes have been found to be both positive and negative. In a short research including 11 patients with type 1 diabetes, a KD improved blood glucose management[28]. It was observed that KD, however, resulted in more frequent and severe hypoglycemia episodes (6.3 incidents per week as opposed to the usual 1-2 episodes per week observed for individuals following conventional or other specific diets). The vast majority of patients also experienced dyslipidemia. Since diabetics already have a higher risk of cardiovascular events, lipid alterations are particularly problematic in this population[28]. Ketone synthesis is increased and ketone clearance is decreased as a result of metabolic abnormalities linked to type 1 diabetes. Compared to people with normal ketone levels, those with excessive ketones are more likely to develop issues of the brain, kidney, liver, and microvasculature. According to

Leow et al., [28] and Schneider et al., [29], type 1 diabetes hyperketonemia is linked to oxidative stress, inflammation, NAFLD, and insulin resistance.

Type 2 Diabetes Management

In the short term, ketogenic diets suppress hunger, encourage weight reduction, lower blood glucose levels, and lower HbA1c[30]. They recycle hemoglobin and glycated glycerides. In the aforementioned metabolic ward trial, 17 overweight or obese yound adults received a baseline diet (50% carbohydrate) for 4 weeks, then a ketogenic diet (5% carbohydrate) for 4 weeks. While fasting insulin and triglycerides dropped, total cholesterol, low density lipoprotein cholesterol (LDL-C), and C-reactive protein rose significantly during the ketogenic diet phase. Some studies have demonstrated improved insulin sensitivity, but this effect seems to depend on fat mass loss[31]. Insulin sensitivity was hampered when participants on the ketogenic diet were tested with a meal that contained 50% carbohydrates from a baseline diet. According to Subramaniam et al., [32] the plant-based diet had a higher glycemic load than the KD, which naturally led to higher postprandial glucose and insulin levels.

On the ketogenic diet, high-sensitivity C-reactive protein, a marker of inflammation, did not differ statistically from baseline; however, on the plant-based diet, it was considerably higher (2.1 vs. 1.2 mg/L; $p = 0.003$). In healthy men, the ability of insulin to restrict endogenous glucose production was reduced by a ketogenic diet (83% fat, 2% carbohydrates). Hemoglobin A1c levels can be decreased by low-carb diets, according to a recent meta-analysis[33].

Other clinical trials utilizing ketogenic diets frequently reduce or eliminate the use of diabetes medications. The benefits of ketogenic diets for people with type 2 diabetes are mostly due to weight loss, and these benefits seem to fade over time. Few further negative consequences on global health measures have been observed in short-term type 2 diabetes research. Thermic protein impact, energy cost of metabolic processes, elevation of satiety hormones, and decreases in insulin resistance, hepatic lipogenesis, inflammation, and reactive oxygen species are further effects it has on persons with type 2 diabetes[34].

Cardiovascular disease

It is crucial to consider how low-carbohydrate diets impact plasma lipid levels. It has long been established that any weight loss program lowers total cholesterol by 2 mg/dL for each kilogram of body weight reduced. Low-carbohydrate diets, however, are usually an exception to this norm. A recent meta-analysis of five investigations found that ketogenic diets had no appreciable effect on LDL-C in those with type 2 diabetes[35]. Despite significant weight loss, LDL-C in the ketogenic group increased by 35% ($p = 0.048$) from 114 mg/dL at baseline to 154 mg/dL at 12 weeks[36].

Some contend that if the rise is predominantly in larger LDL particles, higher LDL-C or LDL particle concentrations are insignificant. Regarding LDL, there are two possible theories. The first is that it may aggravate conditions while also having atherogenic potential.

This worry is supported by data from the Women's Health Study, a low-dose aspirin and vitamin E randomized, placebo-controlled experiment. The size of LDL particles was evaluated as part of the investigation. The risk of incident cardiovascular disease increased by 44% according to the hazard ratio for big LDL particles, which was 1.44. It was 1.63 (a 63% higher risk) for small LDL. Both of them showed statistical significance. In other words, although to a lower extent than small LDL particles, big LDL particles were substantially atherogenic.

It has failed to demonstrate a benefit in terms of reduced cardiovascular risk in studies using HDL-elevating medications or Mendelian randomization trials. In the first group, studies are conducted on people who have naturally occurring genetic variations linked to higher plasma HDL-C concentrations. These genetic characteristics do not reduce the risk of myocardial infarction unless they also lower LDL-C[37].

There are numerous ways the ketogenic diet can treat CVDs. Ketogenesis causes the cataplerotic situation of heart failure. Therefore, ketones are utilized to detect heart failure. KD can allow the body to enter the cataplerotic phase without inducing heart failure since it balances the anaplerotic and cataplerotic flow due to the low amount of carbohydrate present[38].

CONCLUSION

Ketogenic diet has the ability to elicit various cellular responses. It has the ability to ameliorate cardiometabolic conditions with minimal side effects that can be managed. There is a marked impact of Ketogenic diet on selected cardiometabolic related diseases. Controversy surrounding the role of high fat content in KD is based on the fact that diets with high saturated fat and trans fat have higher risk of cardiovascular disease. Replacing these fats with mono and polyunsaturated fat helps to maintain a normal lipid profile. There is therefore a need to explore ways of incorporating it in the management of cardiometabolic diseases to effectively reduce disease burden and economic cost.

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