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# Ketogenic Diet (KD): A Short Review

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**ABSTRACT**

Ketogenic Diet (KD) is defined as a diet of a high-fat and low-carbohydrate intake. It was first used in 1920 for managing epilepsy but it has gained its popularity because of its effect on weight loss. When a person consume less than 50g of carbohydrates per day, the body will begin 2 processes, gluconeogenesis and ketogenesis. Ketogenesis will induce ketosis, which is defined as an elevated serum levels of ketone bodies circulating in the blood. Nutritional ketosis is described by the levels of ketone levels of 0.5 - 3mmol/L. There are 4 major types of ketogenic diet, which are the Classic Ketogenic Diet (CKD), the Medium Chain Triglyceride Ketogenic Diet (MCTKD), the Modified Atkins Diet (MAD), and the Low Glycemic Index Treatment (LGIT). Before initiating KD, there are some contraindications that needs to be ruled out. KD interestingly thought to have some benefits in health condition, such as supporting weight loss, reducing Cardiovascular (CVD) risk, improving serum levels of patient with Type 2 Diabetes Mellitus (T2DM), and also considered as a therapeutic regiment for neurological disorder. However, there are also some evidences mentioning common side effects and concerns in KD, including the "keto flu", kidney problems, disruptions in lipid metabolism, and its questionable adherence to maintain long stable weight loss.



## 1. INTRODUCTION

A ketogenic diet (KD) is a high-fat, low-carbohydrate diet, with an adequate protein intake that was first used in 1920 for managing epilepsy. But in the last decade, this diet became more popular on behalf of its effect in weight loss. This diet is then used for weight management [1], [2]. It is named ketogenic probably because of its capacity to stimulate ketone bodies (KBs) production by various mechanism in our body. It happens when a person consume less than 100g of glucose in his diet [3]. The most used KD is applied by reducing carbohydrate intake to less than 50g a day with a modifiable proportions of protein and fat intake [4]. Mostly, KD has a normal calorific value based on daily caloric requirement. By reducing carbohydrate intake to less than 10%, it induce ketosis in the body. Ketone bodies are produced in a normal value as it is named "nutritional ketosis" [4]. Recently, KD have shown to have a benefit in metabolic syndrome, neuromotor and neurocognitive functions, etc [4].

### 2. History and Origin

KD is first known because of its effect on management of refractory seizures in pediatric patient, found by

Dr Russel Wilder in early 1920s and used as an antiepileptic agents. But it has gained its popularity in the last decade because of its effect on weight loss [1], [2], [5], [6]. Overweight and obesity is a major health problem. It correlates with dyslipidemia and it can lead to cardiovascular disease (CVD) and type 2 diabetes mellitus (T2DM) [7], [8]. A way to treat T2DM is to do diet modification [8]. Hypocaloric diet has popularly used, and shown to cause weight loss. But isocaloric high fat low carbohydrate (HFLC) diets may support blood glucose control better than the traditional high carbohydrate low fat (HCLF) diet, and also improve CVD risks [7], [9].

**3. Physiology and Biochemistry**

The body originally use carbohydrates as the primary source of energy. On average, a person needs 45% carbohydrates, 35% fats, and 15% protein to fulfil his daily intake of macronutrients [10]. But when the body is deprived of carbohydrates, it will begin two processes, which are (1) gluconeogenesis, and (2) ketogenesis [6], [8], [11]. When a person consume less than 50g of carbohydrates per day, it will decrease glucose supply to the liver, brain, and muscles, leading to a decline in glycogen (glucose store). Gluconeogenesis is a process of producing glucose, especially in the liver. This production of the glucose comes from lactic acid, glycerol, and the amino acids (alanine and glutamine) [6], [10]. After 12-24h of fasting, the endogenous glucose production is not enough to meet body requirement and the central nervous system (CNS) requires energy source, hence, insulin levels will decrease and simultaneously, glucagon levels will increase [10], [12], [13]. Reduce levels of insulin will cause a decreased in fat and glucose storage. The KD is beneficial in this stage for maintaining weight and reduce diabetes risk factors [10]. Insulin reduction impact metabolic pathway in the liver and cause hormonal changes that lead to a metabolic switch, which increases the breakdown of fat from the fat cells, resulting in fat derived ketone bodies by using free fatty acids as energy sources, known as ketogenesis [6], [10], [12], [13]. Ketogenesis is primarily dependent on triglyceride metabolism in the adipose tissue. It is induced to provide alternative source of energy. It produces acetoacetate which is converted into ketone (B-hydroxybutiric acid and acetone) [6], [10], [14].

When intake of carbohydrate is enough to meet body requirement, the glucose will be stored in the liver and muscles. But when the body enter a fasting stage, blood glucose will be produced by breaking down glycogen from the liver. It is regulated by the hormone insulin and glucagon. Low insulin levels indicate few fatty acid are stores in the adipose cell, while lipolysis indicate the increased fatty acids in the blood plasma [10], [15].

During the HFLC diet, fasting, starvation, and prolonged intense workout, the amount of glucose is insufficient to maintain glycogen stores in the liver and the muscles, therefore glycogen stores and glucose release are reduced. The glucose is needed primarily in the CNS and Red Blood Cells (RBC). This results in decrease levels of insulin and increase levels of glucagon and adrenaline. Insulin decrease cause an excess supply of fatty acids which leads to ketogenesis. The brain cells are able to use ketones as an alternative fuel [10], [15] (Figure 1).

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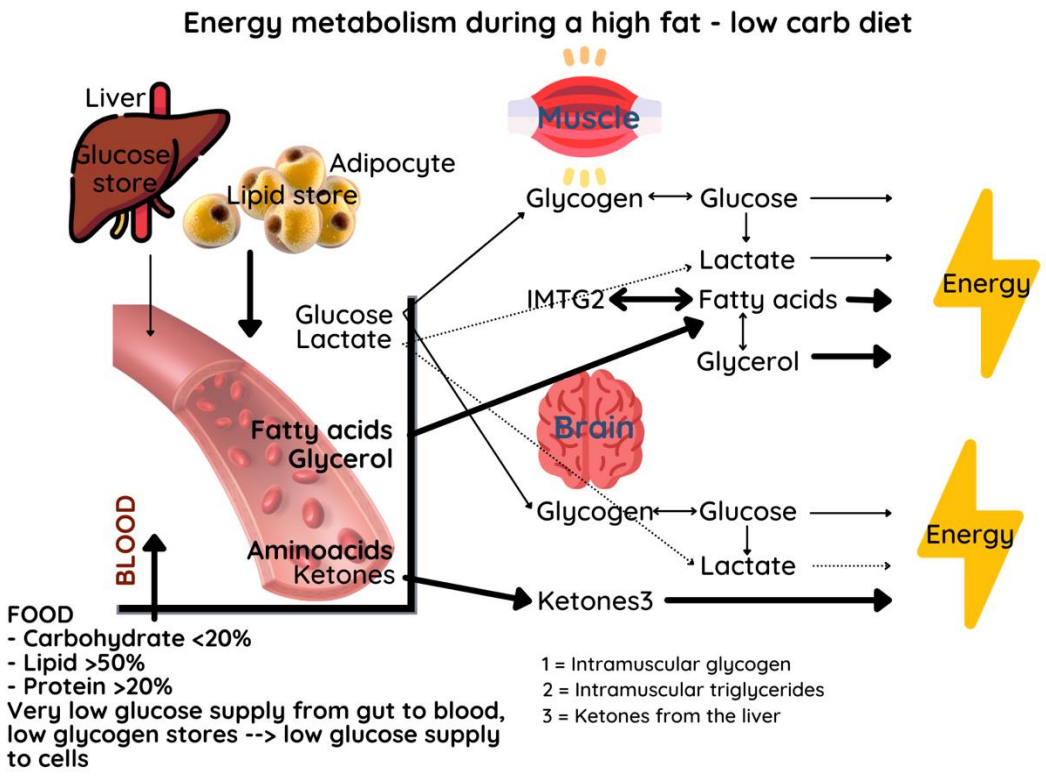


**Figure 1.** Energy metabolism during HFLC diet [10]

Ketogenesis is managed by 3 enzymes: hormone-sensitive lipase (HSL) in the adipocytes, acetyl CoA carboxylase, and HMG CoA synthase (in the liver). It begins with the decreasing amount of insulin (which inhibits ketogenesis) and increasing amount of glucagon (which stimulates ketogenesis) that cause HSL to break down triglycerides into fatty acids. HSL is also stimulated by epinephrine, cortisol, and growth hormone, all of which will be increase during fasting. The fatty acids enters the mitochondria by transforming into acyl CoA through fatty acyl CoA synthase [15], [16]. Acetyl CoA can enter the citric acid cycle only by combining with oxaloacetate, which is produced from the pyruvate during glycolysis. When the body is deprived of glucose, the production of oxaloacetate is preferentially used for gluconeogenesis (Figure. 2), and that leaves acetyl CoA remains in the form of ketone bodies in the mitochondria [10]. HMG CoA synthase lies in the liver mitochondria, function to converts acetoacetyl CoA into acetoacetate (AcAc). Converse to HSL and HMG CoA synthase, acetyl CoA carboxylase is stimulated by increase levels on insulin. It converts acetyl CoA to malonyl CoA, and works by blocking the transport of FFA into the mitochondria [15]. The acyl chains then transported across the mitochondrial membranes via carnitine palmitoyltransferase (CPT-1), and then broken down into acetyl-CoA via B-oxidation [15], [17]. In the liver mitochondria, enzyme m-Thiolase converts acetyl CoA into acetoacetyl CoA (AcAc CoA). Afterward, AcAc CoA is catalyzed by HMGCS2) to generate HMG CoA. HMG CoA is cleaved to liberate acetyl CoA and AcAc via HMGCL. From this step, AcAc is broken down into ketone bodies (acetone and B-hydroxybutyrate) [14], [16], [17]. At this point, there are two mechanisms of energy source usage. The ketone bodies can enter the extrahepatic tissues by being transported from the liver mitochondria, and after reaching the extrahepatic tissues, the two forms of ketone bodies are converted back to the form of AcAc and acetyl CoA to enter the citric acid cycle to produce energy [12], [14], [15] (Figure.3). While on the other mechanism, the remaining ketone bodies that are left in the liver mitochondria can freely diffuse across the cell membranes and it can be used as an alternative energy source for the brain and other tissues [12].

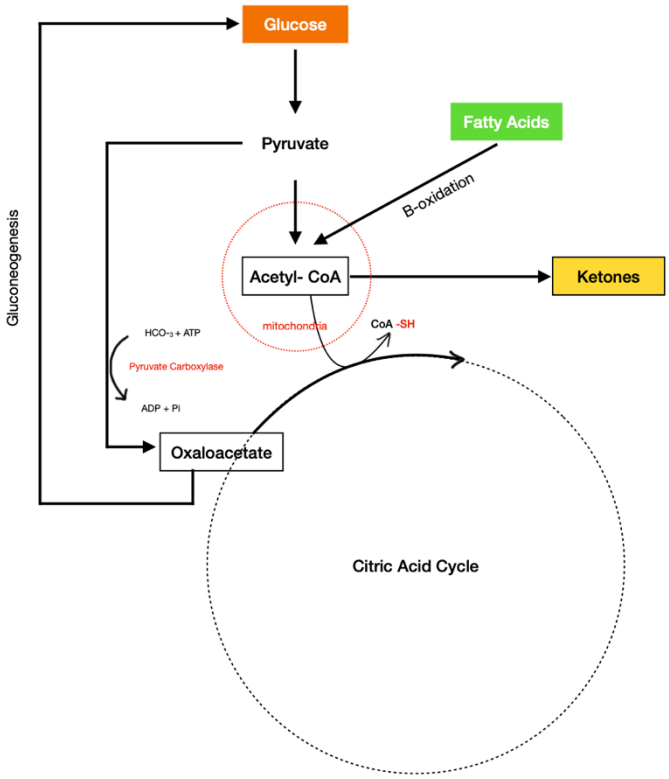


**Figure 2.** The relationship between glucose and fatty acid metabolism

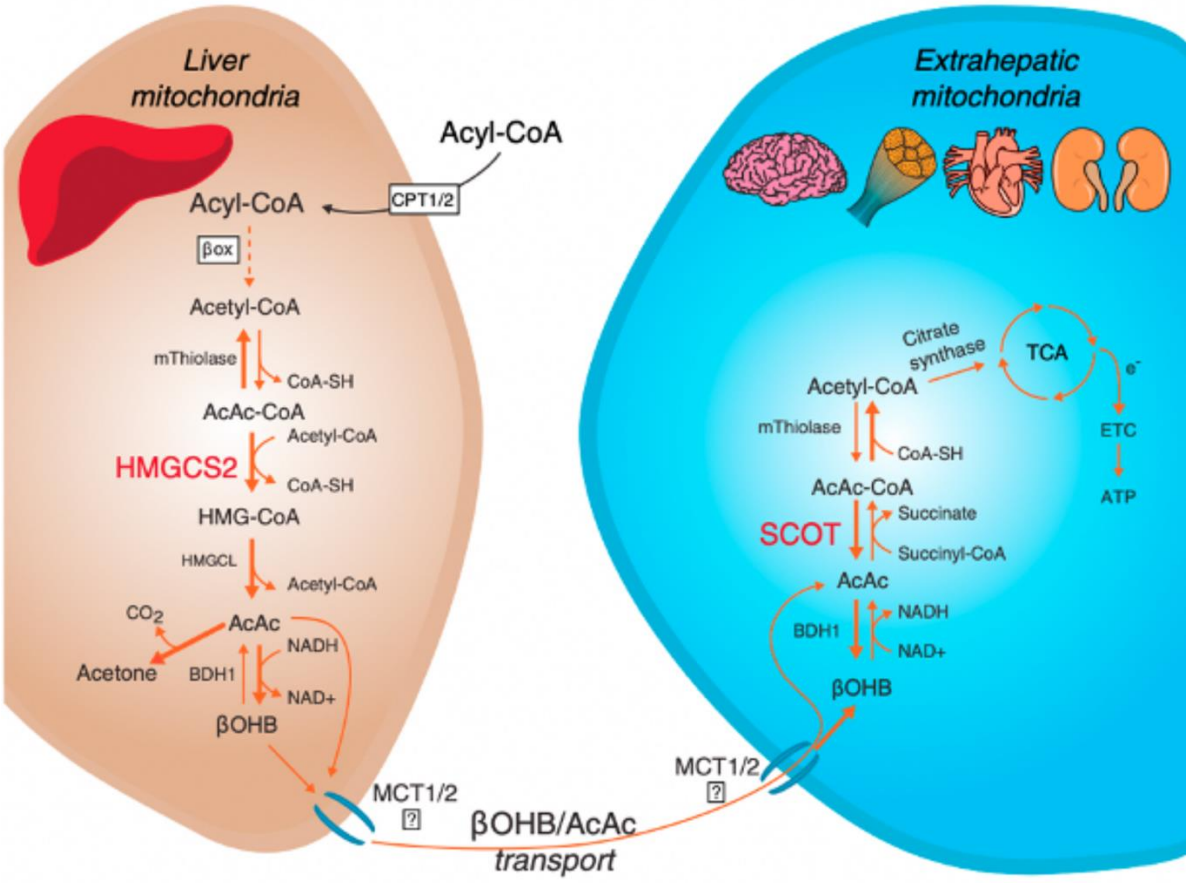


**Figure. 3** Metabolism of Ketone Bodies [22]

**4. Metabolic Changes in Ketosis**

Ketosis is an elevated serum levels of ketone bodies circulating in the blood. Normal levels of ketone bodies is below 0.5 mmol/L [15]. Other study defined ketosis as an increase level of B-hydroxybutyrate to ≥0.3 mmol/L [13]. Ketone bodies is source of energy that can be used in all tissues, including the CNS, because it has a similar binding affinity as glucose [13]. The term ketosis, can either be hyperketonemia or ketoacidosis [15]. In healthy people, ketone levels will not exceed 8 mmol/L because the CNS will begin to use ketone bodies as energy at 4mmol/L. Therefore, this state is referred to as "nutritional ketosis" or "physiological ketosis" [4], [6], [13], [18]. Hypertekonemia is usually caused by prolonged fasting, prolonged intense workout, HFLC diet, and referred to as physiological ketosis. Whereas ketoacidosis is a pathological condition, and usually caused by diabetes mellitus, growth hormone and/or cortisol deficiency, alcohol poisoning, and inborn metabolism error [15]. Ketogenic diet is a HFLC that supress carbohydrate intake to less than 50g per day, although there are some modifications of the classic ketogenic diet. It decrease blood glucose, and glycogen stores in the liver and muscles. By restricting carbohydrates intake for around 24 hours, glycogen store is continue to deplete, insulin production is supressed, stored fat in adipose tissue will begin lipolysis, [18] and the body will enter a catabolic stage and undergoes a metabolic switch to physiological ketosis [6], [11], [19]. Ketogenic diet might give benefits to the body through some aspects. It is considered for treating some health conditions, including its special relevance to oncology by targeting Warburg effect to starve cancer cells, decreasing blood glucose concentrations, to its effect on neurodegenerative and neuropsychiatric disorders [6]. The main goal of doing KD is to achieve a state of ketosis, hence forcing the body to use ketone bodies as the source of energy.

**5. What Makes a Ketogenic Diet? Initiation of a Ketogenic Diet**

A diet induced ketosis, KD, is a physiological ketosis, and it should be distinguished from pathological ketosis [20]. The restriction of carbohydrates causes the body to utilize fat as the primary source of energy, and result in the use of ketone bodies [21]. Ketosis occurs in carbohydrate restriction to below 20-50g/day. There are some variations in KD, each variant is based on its ketogenic ratio (KR), which is calculated by the ratio of the sum of ketogenic factors to the sum of anti-ketogenic factors [13], [22], [23].

KR = (0.9 F + 0.46P) / (1.0C + 0.58P + 0.1F)

F = fat; P = protein; C= carbohydrates

Ketogenesis will occur in KR ≥2 (1.5 as the lowest ketogenic threshold)

Four major types of KDs are: [1], [3], [24- 26]

a. The classic ketogenic diet (CKD), which is the original KD, and is the most restrictive form of KD. CKD use 4:1 or 3:1 lipid and nonlipid (carbohydrates and protein) ratio. KR 4 requires 90% of daily calories intake derived from fat, while KR 3:1 requires 87%. CKD is using long chain triglycerides (LCT) predominantly as the source of fat.

b. The medium chain triglyceride ketogenic diet (MCTKD), is a more liberal KD, which allows more carbohydrate intake compare to the CKD. This diet is composed to up to 60% of medium chain triglycerides (MCT) as its primary source of fat. MCT results in higher ketogenic potential because they do not need digestion and absorption. The MCT do not use bile salts for digestion, instead they are rapidly transported into the portal circulation and eventually converted to ketones in the liver.

c. The modified Atkins diet (MAD) is a KD with KR of 1:1 or 2:1. It allows carbohydrates intake of 10-20g/day, but it does not require gram scales as in CKD. However, its portion is measured by standard household measurement. MAD is easy to apply because it does not require limitation in poritein, fluids, or calories intake.

d. The low glycemic index treatment (LGIT). It allows carbohydrates intake to 40-60g/day as long as it is limited to glycemic index <50.

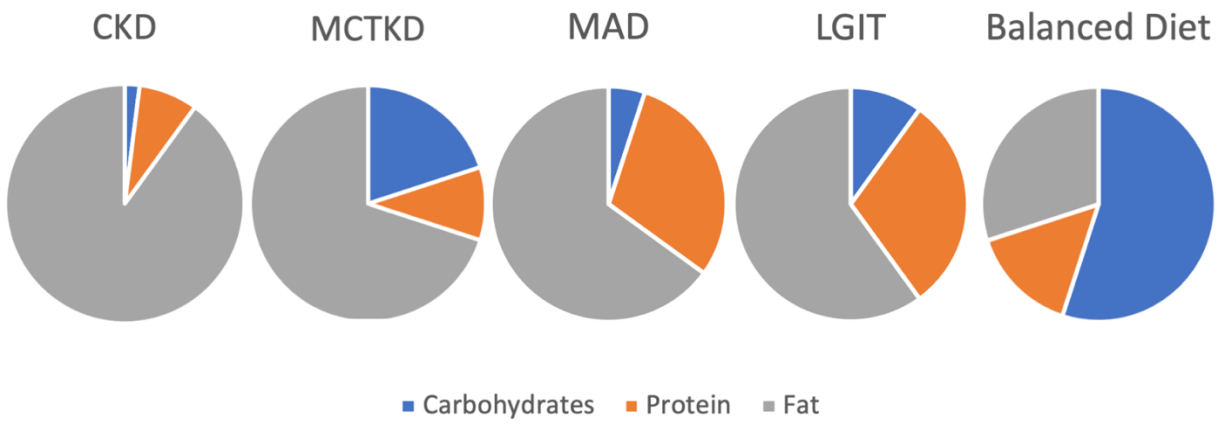


**Figure 4.** Proportion of calories provided by fat, protein, and carbohydrates in the different variants of KD compared to a typical balanced diet [22]

Instead of focusing on what to eat, ketogenic diet is rather focus on what not to eat. Table.1 describes some examples of foods that allowed in KD: [20], [22], [24]

| Food Categories | Examples |
|---|---|
| Vegetable Oils | Olive oil, sunflower oil, wheat, germ oil, rice oil, coconut oil |
| Nuts | Macadamia nut, nut, hazelnut, almond, pistachio nut, peanut, pecan |
| Fruits | Green oilives in brine, avocado, coconut, berries (blackberry, raspberry, strawberry, blueberry) |
| Cheese | Mascarpone, spreadable cheese, brie, gorgonzola, robiola, cheddar |
| Fish | Eel, mackerel, salmon, sardines (canned in oil, or drained), tuna |
| Meats, unprocessed | Beef, lamb, pork, poultry (turkey, duck, chicken) |
| Processed meat | Sausage, mortadella, bacon, wurstel |
| Vegetables | All green leafy vegetables, cruciferous, above the ground vegetables (cauliflower, cabbage, broccoli, zucchini) |
| Animal fats | Pork lard, cow butter, cream from cow's milk with 35% lipids, Greek yogurt |
| Eggs | Hen's egg yolk, Hen's whole egg |
| Drinks | Water, coffee, tea, bone broth |
| Veggie products | Seitan, veggie bacon, tofu, tempeh, soy |
| Miscellaneous | Mayonnaise sauce based on sunflower oil, coconut flour, tofu |

It is important to know the contraindications for doing KD before initiating the diet. People with diabetes and taking insulin or any oral hypoglycemic drugs might be experiencing hypoglycemia. Therefore, it is crucial to adjust the medicines before initiating KD. People with a history of metabolic disorders that limit fat metabolism should not initiate KD. KD is contraindicated in people with inborn disorders of fat metabolism, pancreatitis, primary carnitine deficiency, liver failure, palmitoyltransferase deficiency, carnitine translocase deficiency, porphyrias, or pyruvate kinase deficiency [6], [11], [26].

**6. Possible Benefits of Ketogenic Diet**

Ketogenic diet has become a topic of interest during the recent years, because of its increasing potential role in health accumulated in the literature. There are numerous animal and human studies discussing about the

use of ketogenic diet, such as its role on epilepsy therapy on children, brain injuries [2] alongside many other data suggesting about its influence in metabolic pathways [5]. However, there are also some concerns and side effects mentioned in ketogenic diet [1], [2], [15], [27].

### *6.1 Ketogenic Diet and Weight Loss*

Overweight or obesity is rising over time, and it has negative impact on health because it associated with several health issues that increase cause of mortality, such as cardiovascular disease, type 2 diabetes mellitus (T2DM), metabolic syndrome, hypertension, arthritis, and various cancers [28]. Weight loss is critical to overcome obesity [26]. A considerable numbers of dietary modification are developed to achieve weight loss, even though the most effective diet modification or nutritional approach on behalf of its health benefit both in short and long term, and adherence is not yet determined [28], [29]. High carbohydrates low fat (HCLF) diet has become the most popular dietary strategy to achieve weight loss. But according to some studies, this type of diet is only benefit in weight loss and suffer from long term compliance [29]. In fact, it is a dietary pattern with absolute intake of carbohydrate, and is strongly related to metabolic syndrome and the risk for CVD [30]. A calorie restrictive diet is used to lose fat mass and to improve metabolic health. However, caloric restriction results in resting basal metabolic rate and losses of lean muscles [31]. Therefore, ketogenic diet has become a diet of interest, as it shows to be effective in reducing obesity, hyperlipidemia, and other CVD risk factors [29]. A study shows that there is a significant changes in anthropometric and body composition measurements, and also an average weight loss. This weight loss may be caused by several reasons, which are:

a. increase satiety from protein intake that leads to reduce appetite, allowing a lower energy intake without hunger
b. reduction in lipid synthesis and increased lipolysis mechanism, [29]
c. and a specific metabolic advantage. This includes 3 mechanisms, including protein intake that cause increase thermogenic effects, protein intake that cause higher turnover of gluconeogenesis, and loss of energy via excretion of ketones from the urine and sweat [20].

A review of the effects of Ketogenic Diets on CVD factors mentioned that this benefit of weight loss is caused by increased energy expenditure [32]. Finally, a study has reported that there is a significant reductions in visceral adipose tissue(VAT) and intramuscular adipose tissue (IMAT) in older adults with obesity. Interestingly, there is as well maintenance of lean mass. It is possibly caused by a decrease in hepatic glucose production that leads to sparing lean mass [31]. KD stimulates production of ketones that used as an alternative fuel, so the body undergo ketogenesis rather than gluconeogenesis.

### *6.2 Ketogenic Diet and CVD risk*

Dyslipidemia is one of a risk factor for cardiovascular (CVD) [32]. Recent studies have shown evidences of CVD benefits from KD. A meta-analysis of effects of low carbohydrate diets showed that compared to low fat diet, low carbohydrate diet has significantly led to weight loss and greater Triacyglycerols (TAG) reduction, greater increase in HDL cholesterol, and increase in LDL-cholesterol after 6 months to 2 years offintervention [33]. Another study comparing low carbohydrate diet to low fat diet to 278 participants with abdominal obesity/dyslipidemia showed that the low carbohydrate diet significantly decreased the Hepatic Fat Content (HFC) compared to the low fat diet [34]. A study comparing between low, moderate, and high carbohydrate intake diet in obese patients with metabolic syndrome for 4 weeks also mentioned that the low carbohydrate diet was more effective in reversing metabolic syndrome, by reducing triglycerides, HDL, and small-LDL subclass phenotype levels [35]. Although KD potentially increase LDL cholesterol (a risk factor in CVD), it is still debated that the measurement of particle size of LDL is a potential risk of developing CVD [36], [37]. The Scandinavian Simvastatin Survival Study described that the individual with elevated

LDL cholesterol is at lower risk for developing coronary events compared to individual with high triglycerides and low HDL cholesterol [6] KD have been associated to an increasing number of large particle LDL, which contributes to reduce CVD risk factor by decreasing atherogenicity [32]. All of LDL particle subclasses have a different atherogenicity to variable degrees. The small dense LDL is associated with a higher risk of CVD because it enters the arterial intima faster than the larger LDL. It also stays longer in the circulation, hence, potentially increases time exposure between the arterial tissue and LDL particles to undergo oxidation [37], [38]. The structural composition feature of the small dense LDL particle is lack of binding affinity. All of that reasons lead to an increase risk of atherosclerosis [38]. It is also reported that there is a significant reduction in ApoB that are contribute as an atherogenic property leading to CVD, increased number of total LDL (LDL-C) and HDL-C, and reduction in triglycerides (TG) and blood pressure [22], [29], [36], [37]. There is no evidence of association between saturated fat intake and progression of coronary atherosclerosis. The benefit of metabolic effects that caused by KD is the increase in HDL that have protective effect against CVD and also a decrease in TG that indicates a less atherogenic distribution [22].

### *6.3 Ketogenic Diet and T2DM*

Insulin resistance (IR) is a process that primarily happens in T2DM. It causes hyperglycemia because the liver produce excessive amount of glucose [22]. Diet in low carbohydrates has grown in popularity with numerous reports for managing T2DM [39]. Dietary carbohydrate restriction has become the first approach in diabetes management [10]. Reported that in 194 participants with T2DM following KD for 2 years, there was a significant improvement in HbA1c, fasting glucose and insulin, and HOMA-IR [41]. A systematic review described that the KD has successfully reduced HbA1c values and fasting blood glucose in patient with T2DM [22]. It can possibly be explained because KD mimics some medication of diabetes, which is targeting glycemic control. Ketosis induce decreased glycemia, and decrease the level of fasting insulin and insulin resistance [11]. Another study of the effect of the ketogenic diet on glycemic control and insulin resistance on T2DM participants, reported that blood glucose level was decreased after the intervention of KD as well as a decrease in HbA1c to -1.07%. KD is proved to have numerous health benefits to T2DM patients, as it provides energy through fat oxidation. During KD, metabolic starvation is induced. Carbohydrates intake is strictly limited, and the body enters a fasting period [42], [43]. Hence, ketones are produced and released to the blood by transformation of fatty acids. KD causes extreme restriction of carbohydrates, and it reduces glucose absorption in the intestine, and finally it leads to lower glucose levels and its fluctuation in the circulation [42].

### *6.4 Ketogenic Diet and Neurological Disorder*

Several studies show that ketone bodies have a neuroprotective effect for the brain [44]. Since 1920s, ketogenic diet has been being considered to use as a therapeutic regimen for seizure. The efficacy of the classic KD has been strongly effective to treat refractory epilepsy [45]. Moreover, KD has been used in attempt to prevent migraine attack [46], [47]. KD might be a tool to treat certain neurological disorder. A theory suggest that KD may have anticonvulsant effect coming from its ketone bodies (AcAc and B-hydroxybutyrate), and it results in changes in lipid membrane of the nerve cells or the production of neurotransmitter [47]. Cochrane systematic review concluded that KD is effective for decreasing seizure frequency and severity in children and adolescents with refractory epilepsy [48]. It is also mentioned in a study of Effects of MCT-based ketogenic formula on Alzheimer's disease (AD) patient, that chronic consumption of KD (2-3 months) has improved cognitive function in AD patient. The exact mechanism is still unclear, but it is suggested that AD patients have an impaired glucose utilization and insulin resistance in the brain. Under the period of fasting (ketogenic diet), the brain will use ketones as its primary fuel. And by that mechanism, ketones reduce insulin resistance and metabolic dysregulation [44]. KD may have

another potential effect on neurological disorder. The brain cancer cells have an alter metabolism, that is called “Warburg effect”, or aerobic glycolysis [49]. Tumor cells undergo a high rate of glycolysis that lead to secretion of more lactic acid to meet energy requirement, regardless of the availability of oxygen. KD cause hypoglycemic condition, leading to increase rates of fatty acid oxidation to produce ketonebodies. The normal cells are able to use ketone bodies as an alternative fuel, but unlike normal cells, the tumor cells are not flexible to use ketones bodies, conversely, they require glucose. Therefore, the KD may target Warburg Effect in glycolytic tumor, such as glioma, without toxicity to normal cells [6], [49], [50]. KD also could significantly normalize the habituation deficit on migraine. It is proved to improve migraine clinical feature [51]. There is evidence of an association between migraine, obesity, and metabolic syndrome. Migraine is a condition that lack of excitatory and inhibitory balance, and lack of cortical response habituation in response to and somatosensory repetitive stimulations. It leads to cortical excitability [46], [51]. KD potentially affect neuronal plasticity, balance the inhibitory and excitatory neurotransmitters and support neuroprotective effects by its ketone bodies production and glucose reduction [51]. This supports an approach of ketogenic diet on migraine.

**7. Concerns in Ketogenic Diet**

Ketogenic diet has been aimed to have side effects and concerns on human. Much of the risks proposed to be associated with KD have come from some studies. Common problems that linked to KD are:

Short term effects: dehydration, anorexia, nausea, constipation, acidosis, hypoglycaemia [27]. During the first initiation of KD, people usually experience symptoms including headache, insomnia, fatigue, nausea and vomiting, dizziness, muscle cramping, constipation, and low exercise tolerance, referred to “keto flu”. However, these symptoms are temporary and will be resolve soon after a few days of adaptation [1], [21], [22], [27]. Some of these side effects can be managed, for example preventing the dehydration by adequate water intake [21].

Long term effects: severe hepatic steatosis, disruptions in lipid metabolism (including hyperlipidemia), mineral deficiencies, nephrolithiasis and kidney stones, kidney damage, vitamin deficiency, hypoproteinemia, growth inhibition (especially in the young ages)3 and increased redox imbalance [1], [27]. Kidney stones formation is possibly caused by increased in uric acid load [15], [27] and increase calcium loss in the urine. It can impact bone health and increase the risk of kidney stone formation [15]. Kidney damage might potentially be caused of high protein diets, high nitrogen excretion during the protein metabolism, and finally lead to increase in glomerular pressure and hyperfiltration [11].

To achieve long term maintenance of weight loss, permanent lifestyle changes in required. It is shown by changes in eating habits. Although the effect of KD on weight loss in superior compared to the low GI nutrigenetic diet, the adherence of doing KD is more difficult [28]. Another study also mentioned that KD is hard to be maintained for a long periods of time because of its lack on basic foods (ex: rice, sweets) [21]. Furthermore, without a cautious attention to food quality intake, it can also cause adverse effect. In KD, there has been concerned on the opportunity cost of not eating high fiber, unrefined carbohydrates. But this applied to any other macronutrient-focused diet [6]. High fat low carbohydrates in ketogenic diet is also concerned to potentially causing colorectal cancer because of diet high in meat [15].

**8. Conclusion**

In summary, ketogenic diet (KD) is a high fat low carbohydrate diet with a reduction in carbohydrate intake to less than 50g/day. It has been proven to have benefits in health conditions such as supporting weight loss, reducing CVD risk, improving serum levels of patient with T2DM, and also considered as a therapeutic regiment for neurological disorder. However, this diet is not applicable to all conditions. It might be

potentially causing concerns and side effects. Therefore, this diet needs to be understood before being applied. However, more researches are still needed.

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