

## Study the effect of ketogenic diet on weight loss and lipid profile on obese rats

Co-Prof. Waheeba Elfaki Ahmed<sup>1</sup>, Munirah Suliman Al-Meazil\*<sup>1</sup>, Aseel Ali Al-Salamah<sup>1</sup>

<sup>1</sup> College of Agriculture & Veterinary | Medicine | Qassim University | KSA

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**Abstract:** Obesity is defined as a high percentage of body fat, which is frequently associated with a high body mass index (BMI), which links an individual's weight and height. Obesity is a frequent and widespread disease all over the world, affecting both children and adults, male and female. Obesity, as a source of many diseases and health problems, has recently emerged as a severe health issue that necessitates treatment and follow-up. Obesity prevalence in various age groups worldwide, including Saudi Arabia, where the obesity incidence is 59%, and the dangers of obesity-related ailments such as type 2 diabetes, strokes, and heart disease, which leads to Increased medication use with bariatric surgery. The ketogenic diet (KD) has recently become the most popular diet all over the world. As a result, the keto diet comprises eating a lot of fat, a tiny bit of protein, and very little carbohydrates. The goal of this research report is to learn more about the effects of a KD on weight loss and lipid profile. In this study, the qualitative method was applied, which relies on secondary data sources. In this study, we used a range of research that was also conducted by other researchers.

**Keywords:** ketogenic diet, Obesity, lipid profile, weight loss.

\* Corresponding author:

[munirah.suliman339@gmail.com](mailto:munirah.suliman339@gmail.com)

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### دراسة تأثير النظام الغذائي الكيتوني على فقدان الوزن ودهون الدم في الفئران البدنية

الأستاذ المشارك / وهيبة الفكي أحمد<sup>1</sup>، منيره سليمان المزعل\*<sup>1</sup>، أسيل علي السلامة<sup>1</sup>

<sup>1</sup> كلية الزراعة والطب البيطري | جامعة القصيم | المملكة العربية السعودية

**المستخلص:** تُعرّف السمنة بأنها نسبة عالية من الدهون في الجسم، والتي ترتبط غالبًا بمؤشر كتلة الجسم المرتفع (BMI)، الذي يربط بين وزن الفرد وطوله. السمنة مرض شائع وواسع الانتشار في جميع أنحاء العالم. يصيب الأطفال والبالغين، ذكوراً وإناثاً. ظهرت السمنة كمصدر للعديد من الأمراض والمشاكل الصحية في الآونة الأخيرة كقضية صحية خطيرة تستدعي العلاج والمتابعة. انتشار السمنة في مختلف الفئات العمرية في جميع أنحاء العالم، بما في ذلك المملكة العربية السعودية، حيث تبلغ نسبة الإصابة بالسمنة 59%. ومخاطر الأمراض المرتبطة بالسمنة مثل السكري من النوع 2، والسكتات الدماغية، وأمراض القلب، مما يؤدي إلى زيادة استخدام الأدوية مع جراحات السمنة. أصبح نظام الغذائي الكيتوني مؤخرًا النظام الغذائي الأكثر شعبية في جميع أنحاء العالم. نتيجة لذلك، يشتمل نظام الغذائي الكيتوني على تناول الكثير من الدهون وقليل من البروتين وقليل جدًا من الكربوهيدرات. الهدف من هذا التقرير البحثي هو معرفة المزيد عن تأثيرات نظام الكيتون الغذائي (KD) على إنقاص الوزن ودهون الدم. في هذه الدراسة تم تطبيق المنهج النوعي الذي يعتمد على مصادر البيانات الثانوية. في هذه الدراسة، استخدمنا مجموعة من الأبحاث التي أجراها باحثون آخرون أيضًا. الكلمات المفتاحية: نظام الغذائي الكيتوني، السمنة، دهون الدم، إنقاص الوزن.

## INTRODUCTION

Obesity is clinically defined as a body mass index (BMI) of 30 kg/m; nevertheless, BMI is limited as a single clinical diagnostic criterion for obesity. Obese people expend more energy than regular people because they need more energy to maintain their weight (Saleh et al 2022). The ketogenic diet has fat, protein, and carbohydrate amounts ranging from 55% to 60%, 30% to 35%, and 5% to 10%, respectively (Masood et al 2021).

### **Ketogenic diet benefits and drawbacks:**

Since the 1920s, the ketogenic diet (KD) has been utilized as a kind of treatment for uncontrollable epilepsy. (D'Andrea et al 2019), but additional, more recently revealed benefits include weight loss and reversal/control of type 2 diabetes. (McKenzie et al. 2017) It is an important field for research since, clearly, nutritional intervention can minimize dependency on pharmaceutical therapies and bariatric surgery, which would have considerable economic benefits. Recently, the therapeutic application of ketogenic diets in additional disorders has been examined with promising results (Paoli et al 2013).

Obesity and overweight are on the rise in Kingdom of Saudi Arabia(KSA), particularly among women, and are well-known risk factors for coronary artery disease. gathered information from 17,232 Saudi households with people aged 30 to 70 to perform a national epidemiological health study According to the survey, the prevalence of overweight and obesity in Saudi Arabia is 36.9% and 35.5%, respectively. While women are more likely to be obese than males, men are considered to be significantly more overweight. Obesity prevalence in KSA has risen dramatically in recent years as a result of increased fast-food consumption, increased use of autos, elevators, escalators, remote controls, and increased consumption of sugary beverages (Ahmed et al 2014). Excess energy is converted to triglyceride, which is then stored in adipose tissue depots, which expand in size, increasing body fat and promoting weight gain (Chooi et al 2019). Furthermore, adjuvant therapies such as cognitive-behavioral therapy, medication, and even bariatric surgery may be required for the effective management of overweight and obesity (Freire 2020). Based on this, nutritional therapies that simulate fasting periods have been recommended. Significantly low dietary carbs (less than 50 g/day) result in ketones production. Although historically associated with diabetic acidosis, ketones can be found in modest amounts in a variety of physiological situations, including after an overnight fast, after severe physical activity, or in reaction to a protein-rich meal. Many extra-hepatic tissues, including the central nervous system, skeletal muscle, and the heart, then use ketones as fuel (Bruci et al. 2020).

### **Types of ketogenic diets:**

The Standard ketogenic diet (SKD): This is a low-carbohydrate, moderate-protein, high-fat diet. It is normally composed of 70% fat, 20% protein, and 10% carbs.

Cyclical ketogenic diet (CKD): This diet includes periods of higher-carbohydrates in between ketogenic diet cycles, such as five ketogenic days followed by two high-carbohydrate days as a cycle.

Targeted ketogenic diet (TKD): This diet allows for the incorporation of extra carbohydrates during periods of intense physical exercise.

High-protein ketogenic diet (HPKD): This diet has more protein, with a ratio of roughly 60% fat, 35% protein, and 5% carbohydrates, although as can be seen, it is still a very high fat diet.

The cyclical and targeted ketogenic diets are newer additions that are largely employed by bodybuilders or sportsmen (Shilpa & Mohan2018).

### **Ketogenic diet physiology:**

The body mostly uses carbs to produce energy under normal conditions. Insulin works to take glucose-derived energy and store it. Reduced glucose availability causes the body to secrete less insulin. Glycogen, which is glycogen stored as glucose, is initially available for fuel but depletes after three to four days. The most accessible fuel is then stored fat, and the liver can produce ketone bodies by breaking down stored fat into free fatty acids (McGaugh et al 2022). The liver produces two forms of ketones: acetoacetate and 2-hydroxybutyrate. Because ketone bodies are created by the breakdown of fats, ketosis is the most dependable sign of fat loss. Ketosis is a fully physiological process. Hans Krebs was the first to distinguish healthy ketosis from the pathological ketoacidosis found in type 1 diabetes. (Shilpa& Mohan 2018).

As reported by(Singh 2019) Keto flu, upset stomach, headache, lethargy, and dizziness are among the short-term health hazards. Additionally, some people experience diarrhea, dehydration, and difficulty sleeping. Constipation, which affects the majority of keto dieters, is increased by limiting high-fiber fruits, vegetables, and whole grains.

The Mechanism of ketogenic diet (KD) in Reducing Body Weight There is substantial evidence that ketogenic diets are effective for weight loss. Several studies also compared the suggested low-fat diet to a ketogenic diet for weight loss. A further study compared the low-carb diet to the United Kingdom (UK) Obesity Nutritional Guidelines. The low-carb diet resulted in 3x more weight loss over the course of 6 weeks (Alharbi& Al-Sowayan 2020).

## **Methodology**

### **1. Animals and Diet:**

Male mice from the National Institutes that were 12 to 14 weeks old were used. The ketogenic diet (KD) regimen, which was presented as a paste with 7.24 kcal/gm, contained 75.1% fat (composed of saturated, monounsaturated, and polyunsaturated fatty acids), 8.6% protein, 4.8% fiber, 3.2% carbs, 3.0% ash, and less than 10% moisture. The 3.79 kcal/gm pellets in the control regimen had a composition of (65.2% carbs, 18.1% protein, 5.1% fat, 4.8% fiber, 2. Both diets were produced by Bio-Serv. sixteen weeks.

Each week, body weight was measured and all mice were allowed to eat as they pleased. To gauge the mice's food intake, the amount of leftover chow was weighted each week. They couldn't tell any change at all in the dish. Intake in KD mice (47g/mouse/week) compared to control mice (46g/mouse/week;  $p > 0.5$ ) (Ma, D et al 2018).

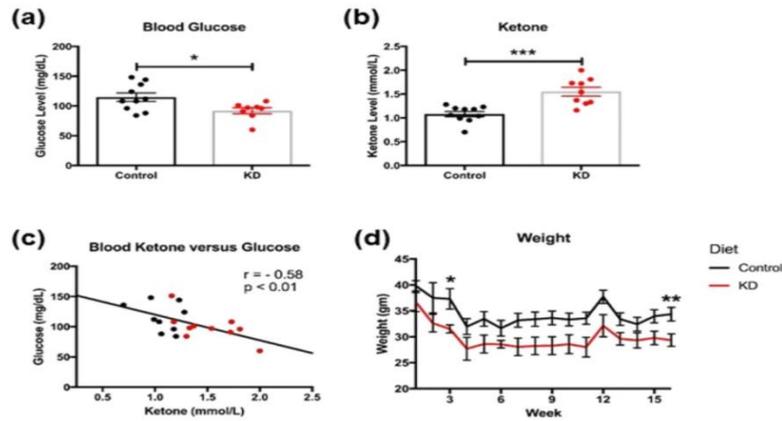
In another research, A high-fat diet (HFD) is one in which fats account for at least 35% of total calories. was administered to mice that were 6 weeks old for 10 weeks, following which they were either switched to a ketogenic diet (KD) or continued on an HFD for an additional 8 weeks. Glucose levels, body fat percentage, and body weight were compared between groups. The expression of proteins and histone post-translational modifications in the liver and kidney were examined using Western blotting, and the expression of genes was examined using quantitative Real-Time polymerase chain reaction (PCR) (Nasser et al 2022). 2. This experimental research was conducted in 2021 on 60 albino mice that were divided into 6 groups (each group containing 10 mice). At the beginning of the experiment, 40 mice were fed a high-fat-high-carbohydrate diet for 12 weeks to enhance gaining weight; then the 4 groups were fed a high-fat-low-carbohydrate diet, while the other two groups were considered as control groups. For sample collection, animals were sacrificed and blood samples were collected for biochemical analysis, tissue samples were taken for histopathological assay. Data were analyzed by SPSS 26 using the ANOVA. (Abed Hussein et al 2022).

## Results

### 1- The ketogenic diet lowers body weight and modifies blood ketone and glucose levels

Blood glucose levels significantly decreased in the mice on the ketogenic diet KD (Fig. 1a; 19.97%;  $p = 0.01$ ). The ketone level of mice fed a KD was significantly higher than that of the control group (Fig. 1b; 43.48%;  $p = 0.0004$ ). It's interesting to notice that there was a strong negative correlation between ketone levels and blood glucose readings (Fig. 1c; Pearson's  $r = 0.58$ ;  $r^2 = 0.33$ ,  $p = 0.01$ ). Another noteworthy result of the current study was that mice on the ketogenic diet lost weight despite consuming more calories per gram (7.24 kcal/gm) than control mice (3.79 kcal/gm). Ketogenic diet mice displayed decreased body weight by week 3 (Fig. 1d; 15.50%;  $p = 0.0096$ ), and this pattern remained for the duration of the study. At the time of the most recent measurement, the weights of the mice on the ketogenic diet were significantly lower than those of the control animals (14.58%;  $p = 0.0042$ ).

Figure 1



The KD reduces body weight while modifying blood ketone and glucose levels. In comparison to control mice, (a) animals on a KD had significantly lower blood glucose levels and (b) significantly higher blood ketone levels. (c) A scatter plot of blood ketone levels and glucose that demonstrates an inverse linear connection (Pearson's  $r = -0.5761$ ,  $p < 0.01$ ) and in which each point corresponds to a mouse ( $n = 19$ ). (d) In comparison to control mice, mice on the KD saw a considerable weight loss over the course of 16 weeks.

The results assertion that a KD lowers blood glucose levels and body weight. (Ma,D et al 2018).

Figure 2

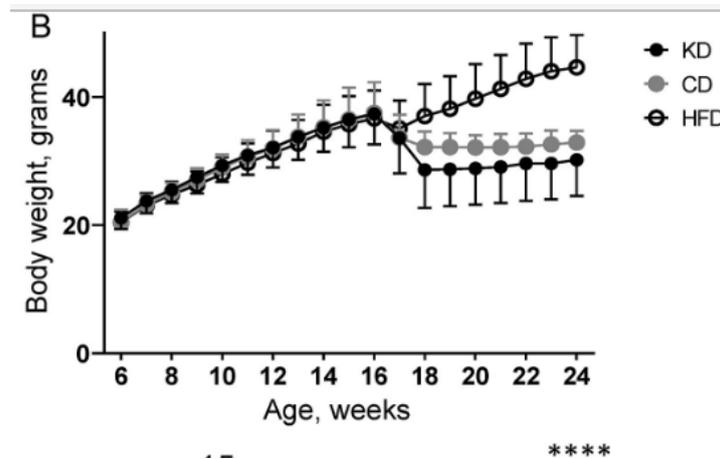
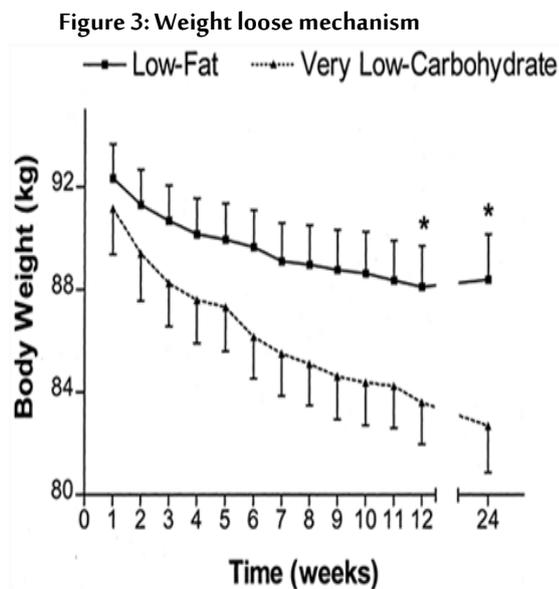


Figure 2. Experimental protocol diagram. (B) Mice's body weight over the course of the investigation. From week 18 to week 24, the area under the curve for body weight was calculated and compared between the three groups using one-way Anova.

After a 10 weeks high-fat diet (HFD) feeding, administration for 8 weeks of a ketogenic diet induced a comparable weight loss and decrease in fat mass (Nasser et al 2022).



The minimum-carb diet produced 3x additional losing weight throughout 6 weeks. Ketogenic diets encourage weight loss (Alharbi & Al-Sowayan 2020).

2- According to the findings of this study, mice fed a high-fat, low-carb diet exhibited elevated blood serum levels of aspartate aminotransferase, alanine aminotransferase, and cholesterol. Additionally, the same groups' lipid and blood glucose levels dropped. In the high-fat, low-carbohydrate diet group, a histopathological study revealed severe fatty changes that caused edema and hepatocyte degeneration in the periportal area due to degeneration of the microvasculature and the formation of bridging fibrosis between the central hepatic lobes and the peripheral area. There were no indications of pathology in the pancreatic tissue samples. (Abed Hussein et al 2022).

## FINDINGS & DISCUSSION

Look into it. (Perticone et al 2019) A ketogenic diet has been shown to be quite successful for weight loss, particularly in reducing fat mass while maintaining fat-free mass. According to (Corrêa et al. 2019), measures to control overweight and obesity do not necessarily need to impose restrictions on certain nutrients, particularly carbohydrates, or boost the intake of food categories whose excessive consumption has been linked to various diseases. (Goldberg et al 2021) Many patients can lose weight by following a low-carbohydrate diet. However, these now-common diets have the potential to aggravate hypercholesterolemia. According to (Choi et al. 2020), ketogenic diets were more effective than low-fat diets in improving metabolic parameters linked with glycemic, weight, and lipid management in patients with overweight or obesity, particularly those with preexisting diabetes. This action could help reduce metabolic dysfunction-related morbidity and mortality in certain patient populations. (Lee, H& Lee, 2021) Ketogenic diets reduced body fat percentage, although athletes with high total cholesterol levels should be watched before starting a ketogenic diet. (Muscogiuri et al 2019). The ketogenic diet is an excellent therapeutic technique for those suffering from obesity, particularly those who have previously tried ineffective diets and/or who urgently need to reduce weight. (Drabińska et al 2021) The outcomes of

ketogenic diet (KD) can be effective for losing weight and modifying body composition without having serious side effects. However, several researches were conducted with a very low-calorie diet, which may impair body weight loss, and the control diets were missing in many studies to date. To summarize, in order to prescribe a KD for weight loss, a more thorough understanding of the safety and physiological consequences of KD in obese persons is required. (Hamdy et al 2018) Low-carbohydrate diets are typically associated with postprandial hyperlipidemia if dietary fat, rather than dietary protein, is used to substitute carbohydrates in these diets.

Indicated. (Becker et al 2021) Human studies of ketogenic diets have yielded conflicting results in cardiovascular disease (CVD) risk variables. The ketogenic diet has been demonstrated to increase Low-density lipoprotein cholesterol (LDL-C) while decreasing triglycerides. Furthermore, KD application in mouse research has shown increased insulin resistance and hyperglycemia.

(Arnold et al 2020) KD mimics the metabolic pathways revealed in calorie restriction. Restriction and endurance This may make it enticing to fads. Dieting culture exists, but the short-term benefits must be assessed. in comparison to the long-term side effects and contraindications the ketogenic diet has been found to result in rapid weight loss of up to 9.6kg in 6 months. Among the physiological alterations related to Very low-calorie Ketogenic Diet (VLCKD) are hypotension, as well as raised high-density lipoprotein (HDL) and low-density lipoprotein (LDL) cholesterol People who are attempting KD can accurately measure their ketone levels to confirm nutritional status. The portable glucometer and the ketone breath test were used to determine ketosis. During the Coronavirus disease (COVID-19) period, the KD has evolved into place of the popular and practical option for rapid weight loss Physical exercise restrictions during the quarantine. According to (Gupta et al 2017), a short-term ketogenic diet followed by nearly carbohydrate-free oral feeding can successfully reduce body weight, waist circumference, blood pressure, and insulin resistance in clinically healthy morbidly obese people (BMI 45 kg/m<sup>2</sup>). In obese hypercholesterolemic patients (BMI >35 kg/m<sup>2</sup>), the diet reduces risk factors for multiple chronic diseases without generating any long-term detrimental consequences in terms of cholesterol, blood glucose, body weight, or body mass index (BMI). In another study, 35 inactive obese persons (13 men and 25 women, aged 7-37 years) with a BMI of 36.1 5.6 kg/m<sup>2</sup> participated in a 12-week KD at the University of Primorska between March and June 2017. Individuals dropped significant amounts of weight (men lost 18 -9 kg, women lost 11- 3 kg), reduced emotional and external eating, felt better about their bodies, and performed better physically as a result of the 12-week KD. In terms of biochemistry, the first two weeks observed a significant decrease in glucose and a significant increase in LDL-C, C-reactive protein (CRP), and Brain-derived neurotrophic factor (BDNF); after that, all of the above parameters returned to baseline. Leptin and insulin levels, on the other hand, were shown to decrease dramatically throughout the course of the 12-week KD. The findings confirm the success of the 12-week KD in terms of weight loss, physical performance, cognitive function, eating habits, and metabolic profile. (Mohorko et al 2019).

## CONCLUSIONS

Based on our review, Ketogenic diets are commonly considered to be a useful tool for weight loss, decreases in blood pressure, triglycerides, and blood sugar, as well as an increase in high-density lipoprotein (HDL). Although the diet has a positive impact on HDL, concurrent increases in low-density lipoprotein C-reactive protein (LDL-C) and very-low-density lipoproteins (VLDL) may raise the risk of cardiovascular disease. Limiting saturated fat should be advocated for those considering the keto diet. In addition, the dietary limitations necessary to maintain ketosis may actually contribute to its short duration.

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