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Ketogenic diet in lactation on body composition and physio-metabolic patterns in adult male rat offspring

Allana Karoline Fernandes Nobre da Silva[1], Esther Maria Monteiro Bispo[1], Fernando Wesley Cavalcanti de Araújo[1], Gisélia de Santana Muniz[1]

[1]Departamento de Nutrição, Universidade Federal de Pernambuco (UFPE) – Recife (PE), Brazil

ABSTRACT

Introduction: The consumption of diets rich in lipids and low in carbohydrates during growth and development has attracted scientific interest, as it may increase the risk of chronic diseases in adulthood. **Objective:** To evaluate the effects of a ketogenic diet during lactation on body weight and food consumption in nursing rats, and its effects on the nutritional and physio-metabolic profile of young adult male offspring. **Methods:** Sixteen Wistar rats and 60 male pups were used. The rats were divided into two groups: Control Group (CG, n=8) with a standard diet and Ketogenic Group (KG, n=8) with a ketogenic diet. The pups were divided into: Male Control Group (MCG, n=30) and Male Ketogenic Group (MKG, n=30). During lactation, the CG received an AIN-93G diet (3.6 calories/g), and the KG received a ketogenic diet (5.4 calories/g, 71% lipids). After weaning, all pups received a commercial diet. Body weight, food intake, and energy consumption were quantified in lactating rats. Body weight, food intake, glucose tolerance and insulin tolerance tests, wet organ weight, serum biochemical composition, and hepatic lipid percentage were quantified in the pups. **Results:** KG had lower food intake but maintained energy consumption. The KGM had lower weight gain and higher blood glucose levels in the tests. In addition, it had lower abdominal fat and higher levels of total cholesterol, LDL, and HDL. **Conclusion:** The maternal ketogenic diet during lactation compromised post-lactation weight gain and abdominal fat in offspring, being associated with increased circulating lipid fractions and impaired glucose homeostasis.

Keywords: diet, high-fat; diet, carbohydrate-restricted; breast feeding; adaptation, physiological; metabolism; abdominal fat.

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Corresponding author: Allana Karoline Fernandes Nobre da Silva - Departamento de Nutrição, Universidade Federal de Pernambuco - Avenida da Engenharia, s/n - Cidade Universitária – CEP: 50740-600 - Recife (PE), Brazil - E-mail: allana.nobre@ufpe.br

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INTRODUCTION

Women's nutritional status during critical periods of development is essential for the baby's health[1]. It is through breast milk that the mother provides the infant with essential nutrients, as well as components that play a role in the development of the nervous and immune systems and in the maturation of the body's other systems[2]. For this to occur, the nursing mother should follow a balanced diet, adequate in macro- and micronutrients, based on natural or minimally processed foods, ensuring the development of physiological systems[3].

Animal studies show that maternal undernutrition or overnutrition—whether occurring during the intrauterine phase and/or extending into the lactation period—can result in offspring with specific alterations in organs and tissues, accompanied by[4,5] compensatory physio-metabolic mechanisms designed to protect tissues, especially the brain.

These adaptations are beneficial for short-term survival but detrimental to health in post-reproductive life[6].

This information is consistent with the Developmental Origins of Health and Disease This information is consistent with the Developmental Origins of Health and Disease (DOHaD) hypothesis and the phenotypic plasticity hypothesis. Both hypotheses relate environmental and genetic factors to susceptibility to chronic noncommunicable diseases environmental and genetic factors to a predisposition to Chronic Noncommunicable Diseases (NCDs)[7]. Thus, genetic predisposition and the environment, especially the nutrients and oxygen received by the mother, can influence the adaptive responses of the developing organism, thereby increasing the likelihood of disease onset in adulthood[8].

Experimental studies in rats using high-fat diets have shown that dietary patterns can influence fetal and postnatal growth. The results vary depending on the period and duration of exposure to the diet[9,10]. High-fat diets are dietary patterns with a high percentage of fat, and the ketogenic diet (KD) consists of extremely high levels of fat and low levels of carbohydrates simultaneously. Thus, the KD can be defined as a low-carbohydrate diet, aiming for a daily intake of less than 50 grams of this macronutrient, and may consist of ~10% carbohydrates, 20% protein, and 60–80% of calories derived from lipids[11]. Notably, this type of very low-carbohydrate diet (≤50 g/day) promotes a dietary regimen like fasting, inducing various changes in human metabolism[12].

Epidemiological evidence indicates that carbohydrate-restricted diets are widely used by postpartum women to accelerate weight loss, showing less weight retention and a better metabolic profile[13]. However, clinical reports of adverse effects, such as ketosis and lactic acidosis in lactating women[14], reveal potential risks and gaps in the physiological understanding of this type of diet during this period; furthermore, the effects of this type of diet on offspring development and health in adulthood have not yet been fully clarified[4,15].

To understand the outcomes of a ketogenic diet (KD) during a critical period of development, with a view toward promoting positive effects on the lives of lactating females and their offspring, this study poses the following guiding question: What are the effects of a ketogenic diet rich in saturated fat during lactation in Wistar rats on body composition, liver fat content, biochemical parameters, and glucose metabolism in male offspring?

The objective of the study was to evaluate the effects of a ketogenic diet in lactating rats on the body composition, biochemical parameters, and liver fat content of their male offspring.

METHODS

Animals

The study complied with the guidelines of CONCEA and the National Institutes of Health Guide for the Care and Use of Laboratory Animals and was approved by CEUA/UFPE (protocol 0053/21). Sixteen nulliparous Wistar female rats were used, housed in polypropylene cages (46 cm × 34 cm × 20 cm) lined with sterile wood shavings in a controlled environment (reversed light cycle, temperature of 22 ± 2°C), with free access to water and feed.

To obtain the newborns, non-inbred males and nulliparous females (90–120 days old) were mated (ratio 1:2), and fertilization was confirmed by vaginal smear and weight monitoring. After confirmation, the pregnant rats were separated and housed individually. During lactation, they were divided into two groups: Control (AIN-93G diet) and Ketogenic (ketogenic diet).

After birth, the litters—standardized to 8 pups (males and females)—were weaned at 21 days, separated into group cages (3–4 animals per cage) by sex, and organized into groups based on the diet received by their mothers. After weaning, the male pups received a standard laboratory diet consisting of commercial Nuvilab feed (Table 1), while the females were assigned to an experimental subgroup of this same study (CEUA/UFPE 0053/21).

Experimental diets

The diets were prepared at the Laboratory of Experimental Nutrition and Dietetics (LNED) in the Department of Nutrition at UFPE. After preparation, the diets were stored under refrigeration at approximately 5°C. During lactation, the Control diet was AIN-93G (3.6 kcal/g), the standard for growing rodents, while the Ketogenic diet (5.4 kcal/g) was formulated based on AIN-93G, with quantitative adjustments to the ingredients and macronutrient ratios to make it high in lipids (71%), moderate in protein (19%), and low in carbohydrates (10%), with the addition of lard and butter, which are rich in saturated fatty acids. In our model, saturated fat accounts for 33.9% of the calories derived from fat per 100 g of diet. After weaning, all pups were fed the standard commercial Nuvilab diet (Table 1).

Experimental groups

The experimental groups were defined by the rats' diet during lactation: Control Group (CG, n=8 – AIN-93G diet) and Ketogenic Group (KG, n=8 – ketogenic diet). After weaning, the male pups were divided into a Male Control Group (MCG, n=30) and a Male Ketogenic Group (MKG, n=30), according to the maternal diet.

Table 1: Macronutrient Composition Based on the Total Energy Value (TEV) of the AIN-93G, Ketogenic, and Nuvilab Diets®

Diets*	Proteins (% of total energy)	Carbohydrates (% of total energy)	Lipids (% kcal of total energy intake)	TEV (kcal/g)
AIN-93G	18	63	19	3.6
Ketogenic	19	10	71	5.4
Nuvilab® **	24	66	10	3.6

*The calculations of the percentage composition were based on the nutritional information provided by the product supplier and on the Brazilian Food Composition Table (TACO).
** Determined by the Adolfo Lutz Institute, 1985.

Tests on lactating rats

Body weight

Lactating female rats were weighed during lactation, on the first and last days, respectively, in the morning between 7:00 a.m. and 10:00 a.m. For this procedure, a Marte XL 500 Class II digital electronic scale with a maximum capacity of 500 g (minimum division 0.001 g) was used to perform the weighing.

Food consumption

Food intake in lactating rats was quantified weekly during the lactation period. Food was collected between 7:00 a.m. and 10:00 a.m. on 5 days each week, and the amount of uneaten feed was calculated by subtracting the remaining feed from the amount provided the previous day. Weekly intake was determined by summing the data from the 5 days of collection per rat, and the total weekly food intake per group was the sum of the data from the rats in each group. Energy intake was calculated by multiplying the amount consumed by the energy value of the diet (Table 1). A Marte XL 500 Class II digital scale with a maximum capacity of 500 g (minimum division 0.001 g) was used for weighing.

In vivo analyses in pups

Body weight and food intake

The pups were weighed at 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, and 21 days of age during lactation. After weaning, the animals' weights were measured at 30, 60, and 90 days of age. At 30 and 60 days of age, the animals' feed intake on a commercial diet was measured over one week, using the same method as for the lactating rats. A Marte XL 500 Class II digital scale with a maximum capacity of 500 g (minimum division 0.001 g) was used for weighing.

Glucose and Insulin Tolerance Tests

At 90 days, the animals underwent two tolerance tests: a glucose tolerance test (GTT) and an insulin tolerance test (ITT), with a 5-day interval between them. In the GTT, the animals were fasted for 12 hours, received 50% glucose (2 g/kg) intraperitoneally, and blood glucose was measured at 0', 30', 60', 90', and 120'. In the ITT, after a 4-hour fast, regular insulin (1.5 U/kg) was administered, and blood glucose levels were measured at 0', 15', 30', 45', and 60'. Blood samples for glucose measurement were collected from the caudal vein of the animals using a sterile needle. A specific colorimetric test (Glicose Bioliquid, Laborclin, Curitiba, Paraná, Brazil) was used to determine blood glucose levels.

Postmortem examinations of the pups - Sample collection

At 100 days postnatal, the animals were euthanized under anesthesia (300 mg/kg ketamine and 30 mg/kg xylazine) and decapitated by guillotine (CONCEA Regulatory Resolution No. 37, dated February 15, 2018). Blood samples were collected, centrifuged at 3,500 rpm for 20 minutes, and frozen at -80°C for biochemical analysis. The following organs were removed and weighed: liver, soleus muscle, and extensor digitorum longus muscle, as well as abdominal and retroperitoneal fat. A Marte XL 500 Class II digital electronic scale with a maximum capacity of 500 g (minimum division 0.001 g) was used for weighing. The wet weight and relative weight of the organs were used for the results.

Biochemical Profile Analysis

The animals' biochemical profile was assessed based on serum levels of glucose, total cholesterol, HDL, LDL, and triglycerides, using an end-point colorimetric assay. The analyses were performed in triplicate using an EPOCH™ spectrophotometer (BioTek®), and Results were expressed in mg/dL according to the manufacturer's specifications. For these procedures, the Liquiform Glucose Kit (REF. 133), Liquiform Cholesterol Kit (REF. 76), Liquiform HDL Cholesterol Kit (REF. 13), Liquiform LDL Cholesterol Kit (REF. 13), and the Liquiform Triglycerides Kit (REF. 87), respectively (Labtest, Lago Santa, Minas Gerais, Brazil). Cardiovascular risk was estimated using the Castelli Indices, calculated as the ratios of total cholesterol to HDL and LDL to HDL, which are predictors of atherosclerotic diseases[16].

Analysis of lipids and lipid content in liver tissue

For the quantitative analysis of hepatic fat, 1,000-mg liver samples were homogenized in 30 mL of a chloroform-methanol solution (2:1) using a mortar and pestle for 2 minutes and 30 seconds. After homogenization, the solution was filtered and transferred to a measuring cylinder, where 1.5% sodium sulfate was added to separate the aqueous and organic phases. 5 mL of the organic phase from each sample, containing the lipid extract, was collected and transferred to pre-weighed sterile containers and evaporated in an oven at 105 ± 5°C for 10 minutes. After cooling in a desiccator, the containers were weighed again, and the amount of lipids from each sample was determined.

Statistical analysis

The data were statistically analyzed using GraphPad Prism 5® software (GraphPad Software, Inc., La Jolla, CA, USA). The Shapiro-Wilk test was used to assess the normality of the data distribution. The data are presented as mean ± standard deviation. Statistical analysis of body weight and food intake in the female rats was performed using a two-way ANOVA with repeated measures, based on the variables assessed and normality, followed by Tukey's post-hoc test. For comparisons between the control group (CG) and the ketogenic group (KG), one-way ANOVA and Student's t-test were used. Analysis of the offspring according to the groups (diet and age variables) was performed using a two-way ANOVA with repeated measures, based on the variables and normality, followed by Tukey's

post-hoc test if a difference between the groups was determined. The significance level was set at 5% ($p < 0.05$).

RESULTS

Assessments of Lactating Rats

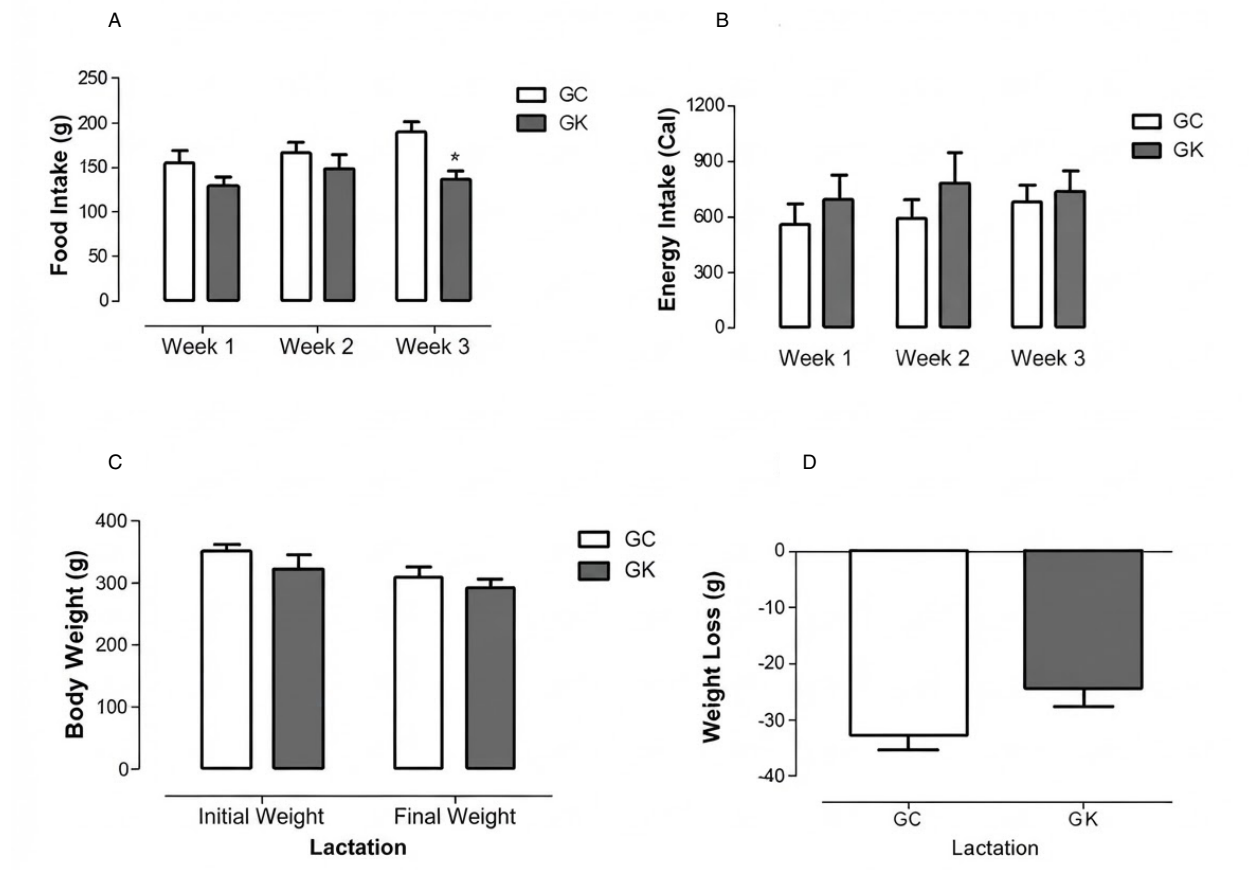
Food intake in the KG group was lower during the third week of lactation compared to the CG group (*p=0.004) (Figure 1A). However, there was no difference in energy intake between the groups (Figure 1B) (p>0.05). Figures 1C and 1D show the initial and final body weights, as well as changes in body weight in the rats during lactation. The KG did not differ in body weight (p>0.05) or weight loss compared to the CG (CG= −27.63±3.88; KG= −13.00±5.00; p=0.08).

Tests on offspring during and after lactation

There were no differences in the body weights of the pups during lactation (Figure 2A). Analyses of body weight at 30, 60, and 90 days of age also showed no differences (Figure 2B). There was no statistically significant difference in weight gain between the MKG and MCG groups during lactation; however, the MKG showed lower weight gain compared to the MCG group from 30 to 90 days of postnatal life (p*<0.05) (Figure 2C). The average feed intake of the groups was analyzed by period (30 to 35 days and 60 to 65 days of age). During the periods evaluated, there was no difference between males in the KG and CG (p=0.451).

Regarding the glucose tolerance tests, the MKG had a higher plasma glucose concentration at the 30-minute time point compared to the MCG; however, when analyzing the area under the glucose curve of the test, no difference was observed (MKG vs. MCG, p=0.68) (Figure 3A).

In the insulin tolerance test, the MKG had higher plasma glucose concentrations compared to the MCG group at most of the time points analyzed: 0', 15', and 30'; however, this was not sufficient to yield statistically significant differences when examining the area under the glycemic curve (MKG vs. MCG, p=0.6965) (Figure 3B).



CG—Control Group (n=8), KG—Ketogenic Group (n=8). Values represent mean ± standard deviation. Food and energy intake, and weight during the lactation period: two-way ANOVA with repeated measures, followed by Tukey's post hoc test. A t-test was used to analyze weight loss during lactation. *p<0.05 between KG and CG.

Figure 1: Food intake (A), energy intake (B), body weight (C), and weight changes (D) in female rats fed a ketogenic diet during lactation.

Postmortem analyses of offspring

The wet weight of abdominal fat was lower in the MKG group compared to the MCG group (p*=0.029) (Table 2).

Regarding biochemical parameters, the MKG group had higher serum concentrations of total cholesterol, LDL cholesterol, and HDL cholesterol compared to the MCG group, while serum glucose and triglyceride concentrations did not differ between the groups. The Castelli risk index (CRI-I and CRI-II) showed no differences between the control and ketogenic groups (Table 3).

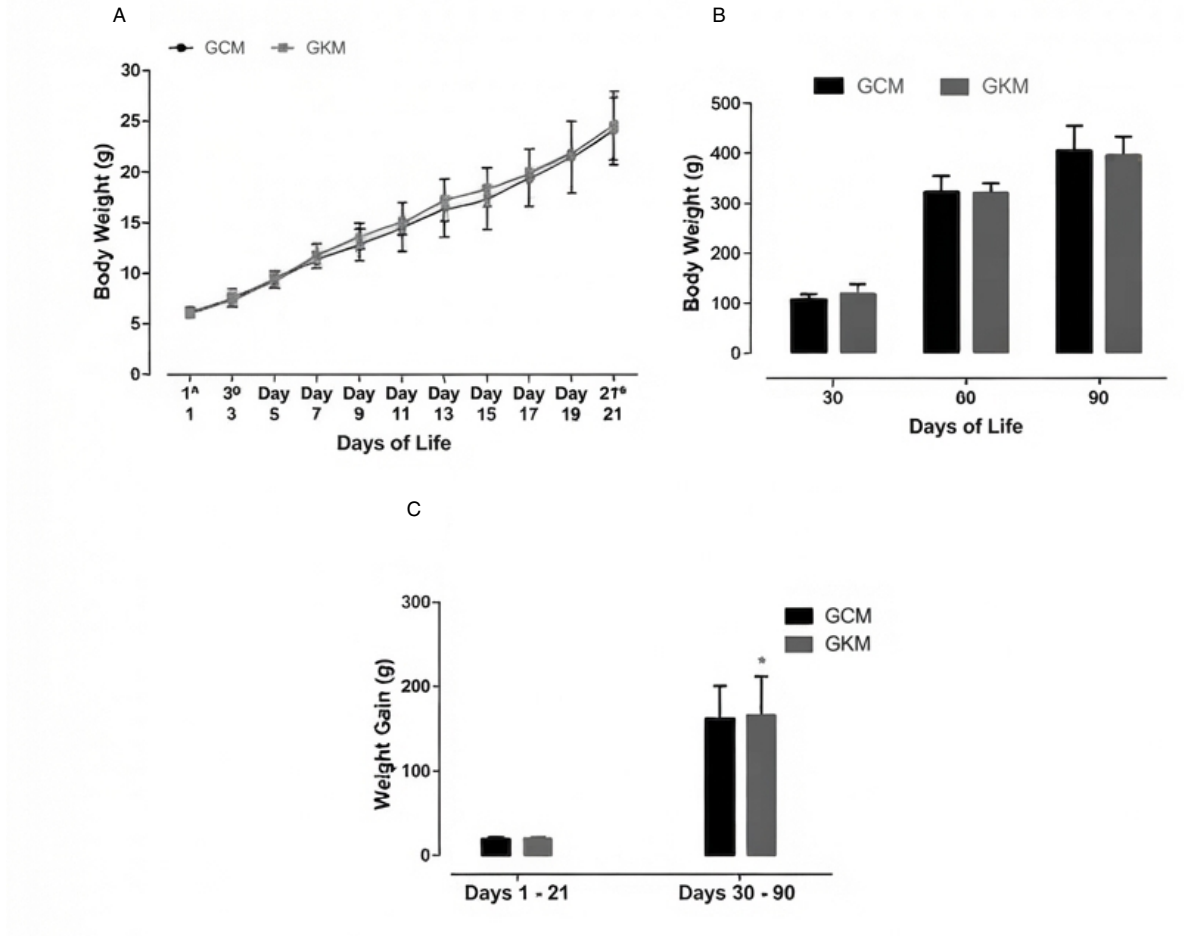
When analyzing the fat concentration (%) in the livers of the offspring, no statistically significant difference was observed between the groups (MKG vs. MCG, p=0.4564).

DISCUSSION

This study evaluated, based on the hypothesis of phenotypic plasticity—which refers to the ability of genes to organize themselves into different ranges of physiological or morphological states during developmental periods, adapting to different environmental conditions and stimuli[8], the effects of a ketogenic diet during lactation on body composition, biochemical parameters, and liver fat content. This dietary model resulted in a significant increase in fat intake, particularly saturated fat, over the course of approximately 4 weeks of lactation.

Low-carbohydrate, high-fat diets are used by postpartum mothers to accelerate weight loss[13], but they can alter maternal metabolism and affect the offspring[15]. In lactating rats, this diet allows for a controlled investigation of maternal effects and metabolic programming in the offspring, shedding light on the mechanisms and potential risks of this practice.

Lactation is an anabolic phase for the synthesis of breast milk, with the mother's dietary pattern influencing lactation efficiency and the body composition of lactating women. Thus, exclusive breastfeeding mobilizes maternal body reserves to provide the



MCG—Control Group—Male Offspring (n=30), MKG—Ketogenic Group—Male Offspring (n=30). Values are expressed as mean ± standard deviation. Weight changes in the offspring during and after the lactation period. Two-way ANOVA with repeated measures followed by Tukey's post hoc test, p > 0.05. *p < 0.05 between MKG and MCG.

Figure 2: Weight changes in the pups during lactation (A), body weight of the pups in the post-lactation period (B), and weight gain in the pups during and after lactation (C).

nutrients and calories necessary for efficient lactation[15]. Lactation causes hormonal changes, leading to weight loss, though this does not follow a linear relationship with breastfeeding[15], This is consistent with the results of this study, which demonstrated that both groups experienced significant weight loss; however, the ketogenic diet did not contribute to greater weight loss, since despite the lower food intake of the KG rats, energy intake was equivalent between the groups due to the higher calorie content of the KD.

High-fat and/or high-calorie diets in pregnant rats reduce the amount of feed ingested but do not affect total caloric intake compared to rats fed a standard diet[4,5], a finding observed in this study. The rats in the KG group consumed less food, due to greater satiety caused by the high fat concentration of the ketogenic diet (KD)[14], which is high in calories (5.4 calories/g) compared to the control diet (3.6 calories/g)[4].

In addition to this satiety-inducing effect, the ketogenic diet promotes increased synthesis and utilization of ketone bodies, which, at high concentrations, increase satiety[17]. The increase in plasma ketone body concentration positively regulates the anorexigenic pathway, reducing levels of brain neuropeptide Y (NPY), which decreases the cholecystokinin (CCK) response to food intake, reduces circulating ghrelin, and decreases food intake[18]. Thus, anorexia increases and decreases in proportion to the degree of ketonemia[19].

The study by Moreno-Sepúlveda et al.[19] reports the existence of a "set point" for body weight in humans and rodents, which can

Table 2: Wet weight of the organs of offspring fed a ketogenic diet during the lactation period.

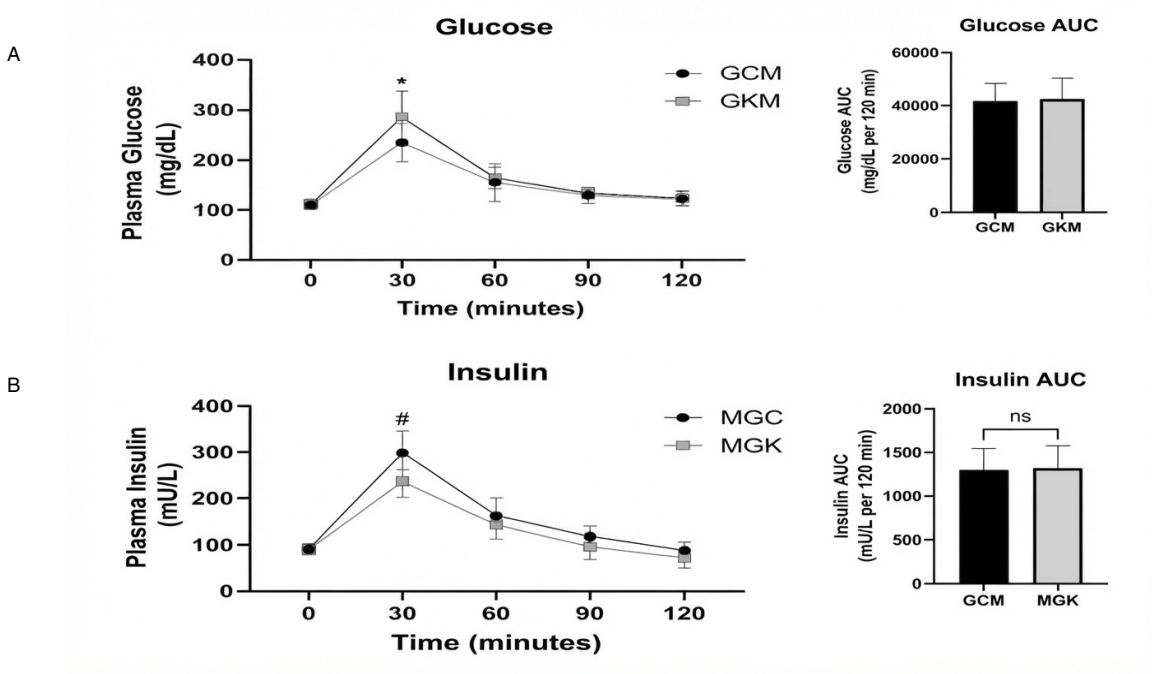
Wet weight of tissues (g)	MCG	MKG	p
Liver (g)	9.36±0.92	8.81±1.10	0.1292
Abdominal fat (g)	3.46±0.99	2.73±0.77*	0.0299
Retroperitoneal fat (g)	3.47±0.80	3.85±0.91	0.2346
Left EDL (g)	0.152±0.03	0.153±0.02	0.9526
Right EDL (g)	0.149±0.03	0.153±0.01	0.6943
Total EDL (g)	0.301±0.06	0.306±0.02	0.4232
Left soleus (g)	0.151±0.03	0.144±0.02	0.4454
Right soleus (g)	0.151±0.03	0.144±0.02	0.8164
Total soleus (g)	0.302±0.05	0.286±0.04	0.3631

MCG—Control Group—Male Offspring (n=30), MKG—Ketogenic Group—Male Offspring (n=30). EDL—Extensor digitorum longus muscle—Values are expressed as mean ± standard deviation. *MCG versus MKG; t-test. *p<0.05.

Table 3: Biochemical parameters of offspring fed a ketogenic diet during the lactation period.

Parameters	MCG	MKG
Total cholesterol (mg/dL)	58.83±6.92	73.13±16.81*
Glucose (mg/dL)	155.1±24.2	140.0±27.4
Triglycerides (mg/dL)	32.58±10.17	38.76±10.02
HDL cholesterol (mg/dL)	35.51±5.24	42.79±10.32*
LDL cholesterol (mg/dL)	10.83±2.47	14.91±6.30*
Castelli risk index I Total cholesterol / HDL cholesterol	1.66±0.02	1.71±0.03
Castelli risk index II LDL cholesterol / HDL cholesterol	0.30±0.01	0.34±0.02

MCG—Control Group—Male Offspring (n=30), MKG—Ketogenic Group—Male Offspring (n=30). Values are expressed as mean ± standard deviation. *P<0.05, MCG versus MKG; Student's t-test. *p<0.05.



MCG—Control Group—Male Offspring (n=30), MKG—Ketogenic Group—Male Offspring (n=30). Values are expressed as mean ± standard deviation. The t-test was used for statistical comparison. Glucose curves from the glucose tolerance test performed at 90 days of age and the insulin tolerance test performed at 95 days of age: *p < 0.05 - MKG vs. MCG.

Figure 3: Glycemic curve and area under the curve (AUC) for the glucose tolerance test administered when the pups were 90 days old (A), and glycemic curve and area under the curve (AUC) for the insulin tolerance test administered when the pups were 95 days old (B).

lead to changes in food intake and energy expenditure to stabilize weight at a specific level and resist deviations from it[20]. It is believed that these mechanisms may explain the effects of KD on the bodies of KG rats, which, when exposed to a high-fat diet with a higher caloric content than they were accustomed to, reduced their food intake at the end of lactation and, consequently, showed no change in body weight.

The Developmental Origins of Health and Disease (DOHaD) model suggests that unbalanced diets during critical periods, such as lactation, may predispose individuals to future diseases by affecting somatic growth, changes in body weight, and even the development of metabolic syndrome[21]. In relation to the results of this study, physiometabolic changes were observed in the offspring due to KD, which did not affect the pups' birth weight but resulted in lower weight gain between 30 and 90 days of age.

The offspring of the KG group showed lower postnatal weight gain, lower abdominal fat mass, and lower soleus muscle mass compared to the MCG group. One factor that could explain these results is that one of the main mechanisms of fat deposition in male animals involves storage within visceral tissues[22]. Thus, this tissue is related to insulin resistance and lipolytic activity, potentially leading to an increase in the amount of circulating fatty acids, which in turn causes increased hepatic glucose production, hyperinsulinemia, and other components of metabolic syndrome[23]. These findings were confirmed in this study, as the MKG group—despite not exhibiting higher wet weight of abdominal fat—showed higher plasma glucose concentrations at most time points during the insulin tolerance test (ITT) and higher serum concentrations of lipid components compared to the MCG group; we will discuss these results in more detail later.

Evidence supports a direct effect of ketone bodies on hormone levels that influence appetite, particularly ghrelin levels[19,24] in this anorexigenic mechanism: as circulating fatty acids increase in the postprandial period, there is a consequent reduction in NPY and circulating ghrelin, accompanied by a decrease in food intake[19,25].

Given the controversy surrounding the relationship between the ketogenic diet (KD), plasma glucose, and insulin sensitivity, we analyzed glucose and insulin tolerance at 90 days of age to understand this connection. Insulin resistance (IR) is the pathogenic link underlying the various abnormalities grouped under the term "metabolic syndrome"[26], affecting energy utilization and promoting fat accumulation in non-adipose organs[27].

The macronutrient composition of the diet, the duration of exposure, and the duration of the dietary intervention may affect pancreatic insulin secretion—whether in a fasting or postprandial state—regardless of body composition[28]. In light of this, studies that also assessed plasma glucose concentrations using glucose tolerance tests found that a high-fat diet, particularly those with a higher percentage of saturated fatty acids[29,30], and simultaneously low in carbohydrates, can decrease insulin sensitivity and increase plasma glucose concentrations, primarily by raising fasting blood glucose levels[29,30], which supports our findings.

On diets high in fat and low in carbohydrates, the metabolism begins to preferentially oxidize fatty acids, leading to the accumulation of lipid intermediates such as diacylglycerol and ceramides, which inhibit insulin signaling and reduce glucose uptake[31]. At the same time, the low availability of carbohydrates stimulates the liver to increase gluconeogenesis, raising endogenous glucose production and contributing to hyperglycemia[32]. Furthermore, excess free fatty acids activate inflammatory pathways and oxidative stress, promoting the inhibitory phosphorylation of insulin signaling proteins, which exacerbates peripheral insulin resistance[33].

Saturated fat intake is associated with damage to mitochondria and cell membranes, promoting the production of malonyl-CoA, which reduces the efficiency of the GLUT-4 glucose transporter[34].

In an experimental study, Oliveira[35] showed that offspring of female rats fed a diet high in saturated fat and low in unsaturated fatty acids during pregnancy and lactation exhibited alterations in blood glucose and insulin levels as adults, with deleterious effects on pancreatic beta cells. The study by Vessby[36] concluded that the quality of dietary fat is crucial in the development of plasma abnormalities, such as elevated glucose levels, highlighting that mono- and polyunsaturated fatty acids not only do not alter glucose levels but also have the ability to reduce diastolic blood pressure.

High-fat diets administered during critical periods of development are associated with increased body fat findings already demonstrated in experimental models involving monkeys, dogs, pigs, squirrels, hamsters, and Wistar rats[37], as well as with the occurrence of metabolic abnormalities, such as hyperglycemia and hyperinsulinemia[38]. An experimental study in male mice demonstrated that a KD is associated with increased SIRT-1 (sirtuin-1) mRNA expression in visceral adipose tissue. SIRTs are nicotinamide adenine dinucleotide (NAD+)-dependent cellular sensors involved in the regulation of mitochondrial energy metabolism. Thus, the higher the expression of SIRT-1 mRNA, the lower the accumulation of adipocytes in white adipose tissue (visceral fat) and muscle[39]. This corroborates the results of this study in the MKG, which showed a lower amount of abdominal tissue and a reduction in soleus muscle weight.

Dietary composition during critical stages of development is a key factor in changes in biochemical parameters[9,38]. In this study, the KD was formulated with lard to increase saturated fatty acids, which may have led to higher HDL concentrations in the high-fat group (MKG) compared to the control group (MCG), as experimental evidence suggests that saturated fatty acids from lard cause a significant increase in the HDL fraction in animals[40]. Furthermore, high-fat, low-carbohydrate diets can increase total cholesterol and HDL, promoting weight gain and the risk of

atherosclerosis, whereas diets rich in polyunsaturated fatty acids administered during the prenatal or postnatal period can result in low concentrations of total cholesterol and LDL cholesterol[39,40].

In summary, the results of this study reinforce the idea that metabolic disorders in adulthood may have their origins in early life. A maternal diet rich in lipids and low in carbohydrates had a significant impact on the adaptive responses of the offspring, altering weight gain, body composition, and glucose and lipid profiles compared to animals in the control group. This highlights the body's plasticity in response to early nutritional insults. Furthermore, this study emphasizes that not only the quantity but also the quality of lipids in the maternal diet plays a crucial role in these effects on the offspring's health.

Conclusion

Maternal consumption of a ketogenic diet rich in saturated fat during lactation led to changes in the offspring's weight gain and body composition in the postnatal period and was associated with increased circulating lipid fractions and altered glucose homeostasis, as assessed by glucose and insulin tolerance tests when compared to animals in the control group. However, the ketogenic diet consumed during lactation did not impair food intake in the offspring during the postlactational period, nor did it influence fat accumulation in the liver tissue of that group.

These findings highlight the impacts of phenotypic plasticity during critical periods of development, which can result in permanent metabolic changes when the body is exposed to early nutritional insults. During periods of heightened sensitivity, adaptive adjustments are made to ensure immediate survival; however, such changes can reprogram metabolism, predisposing the individual to metabolic dysfunction throughout life.

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